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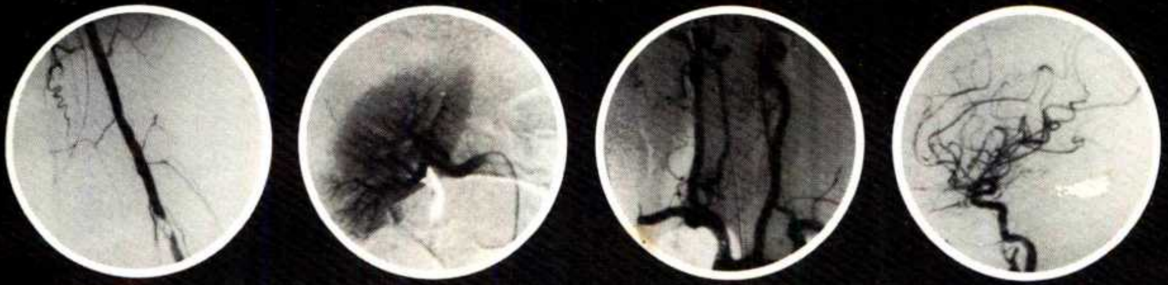

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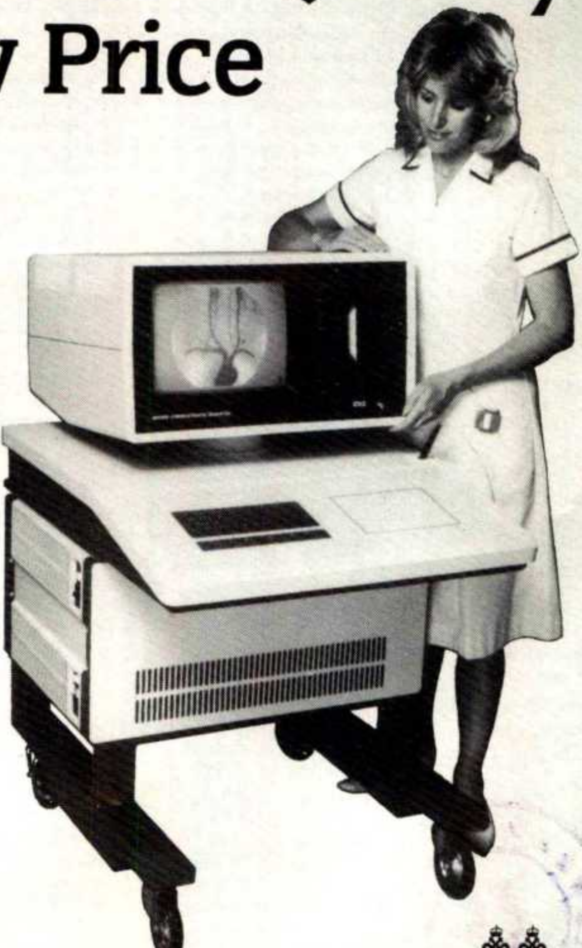

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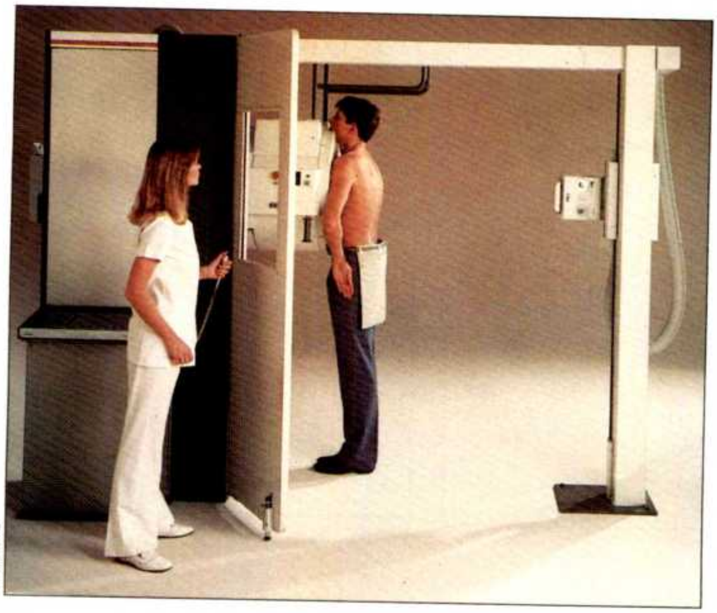

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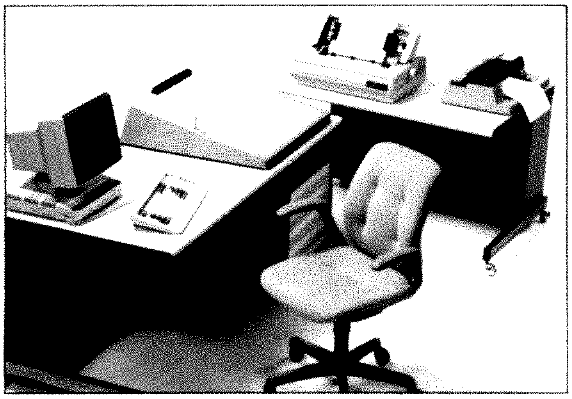

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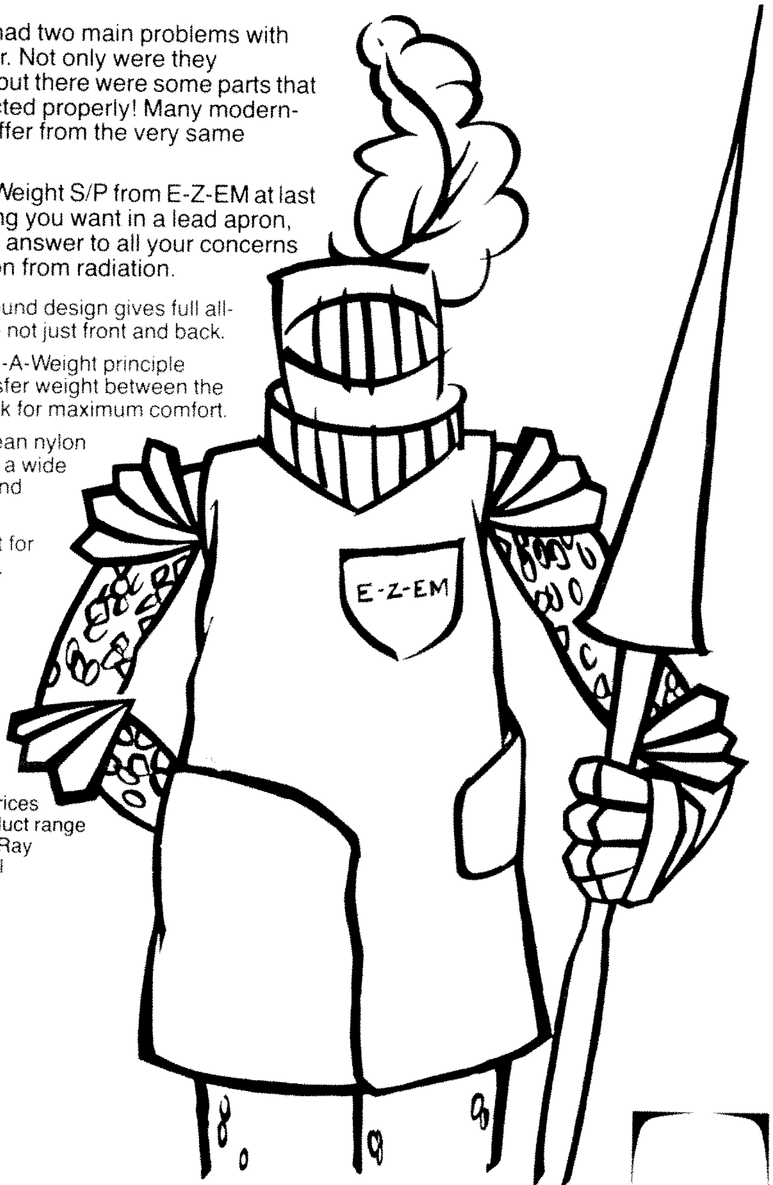

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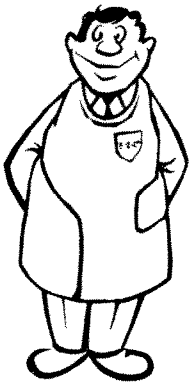

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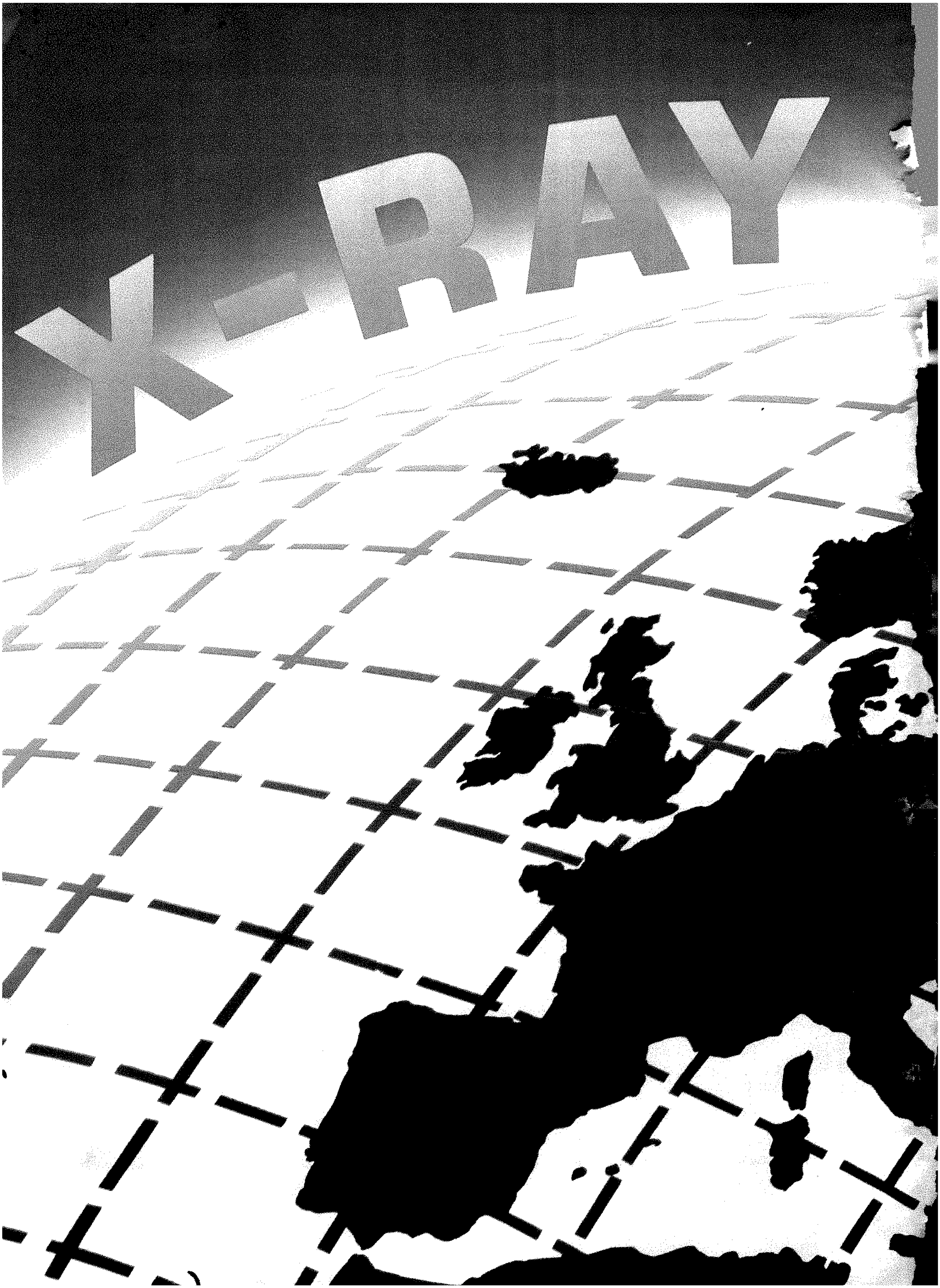
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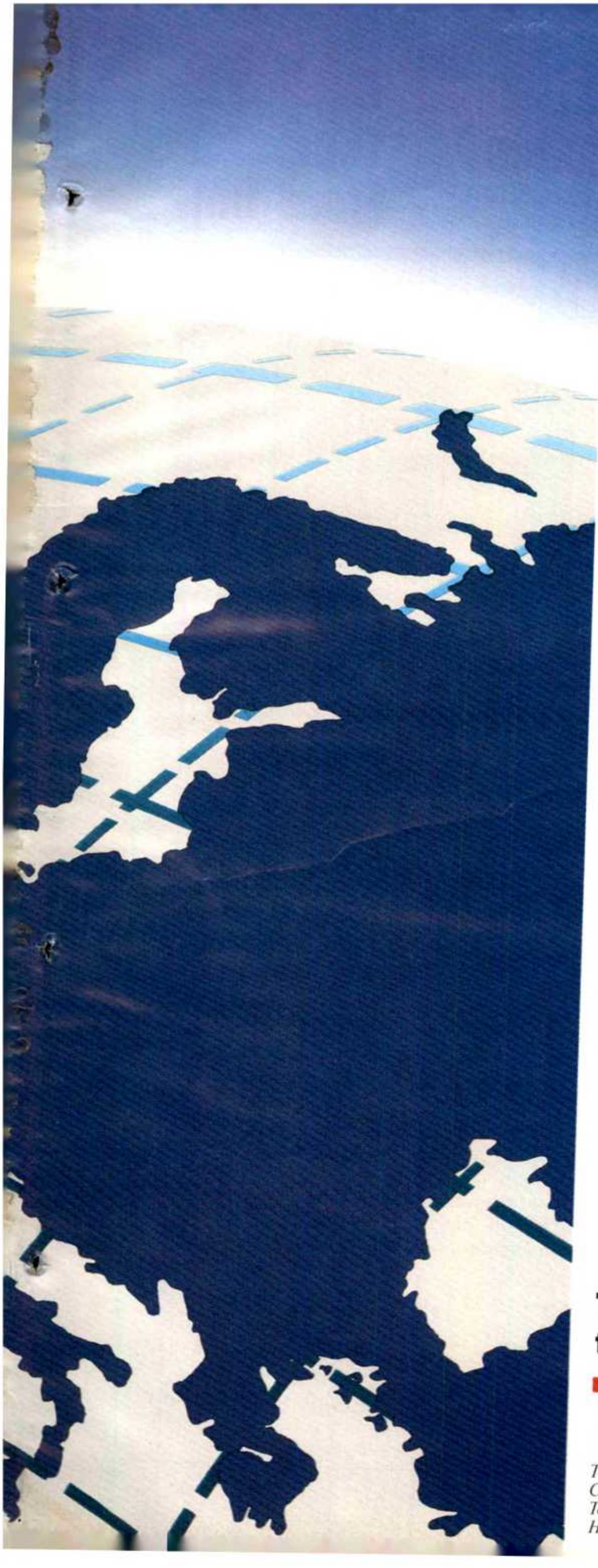

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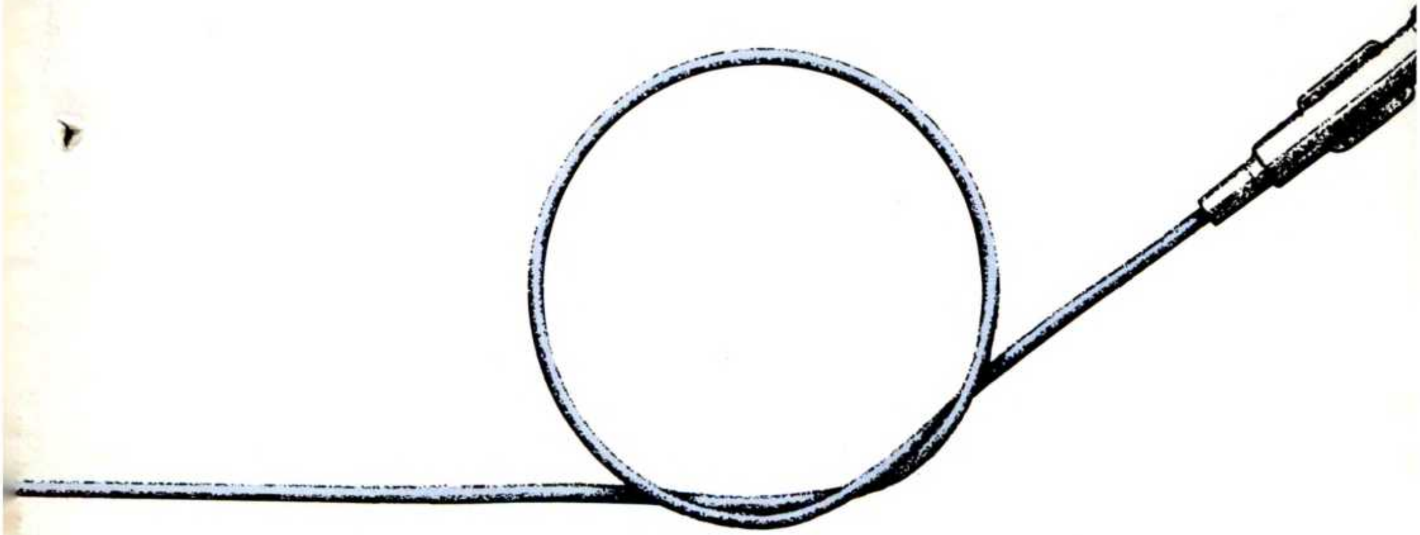

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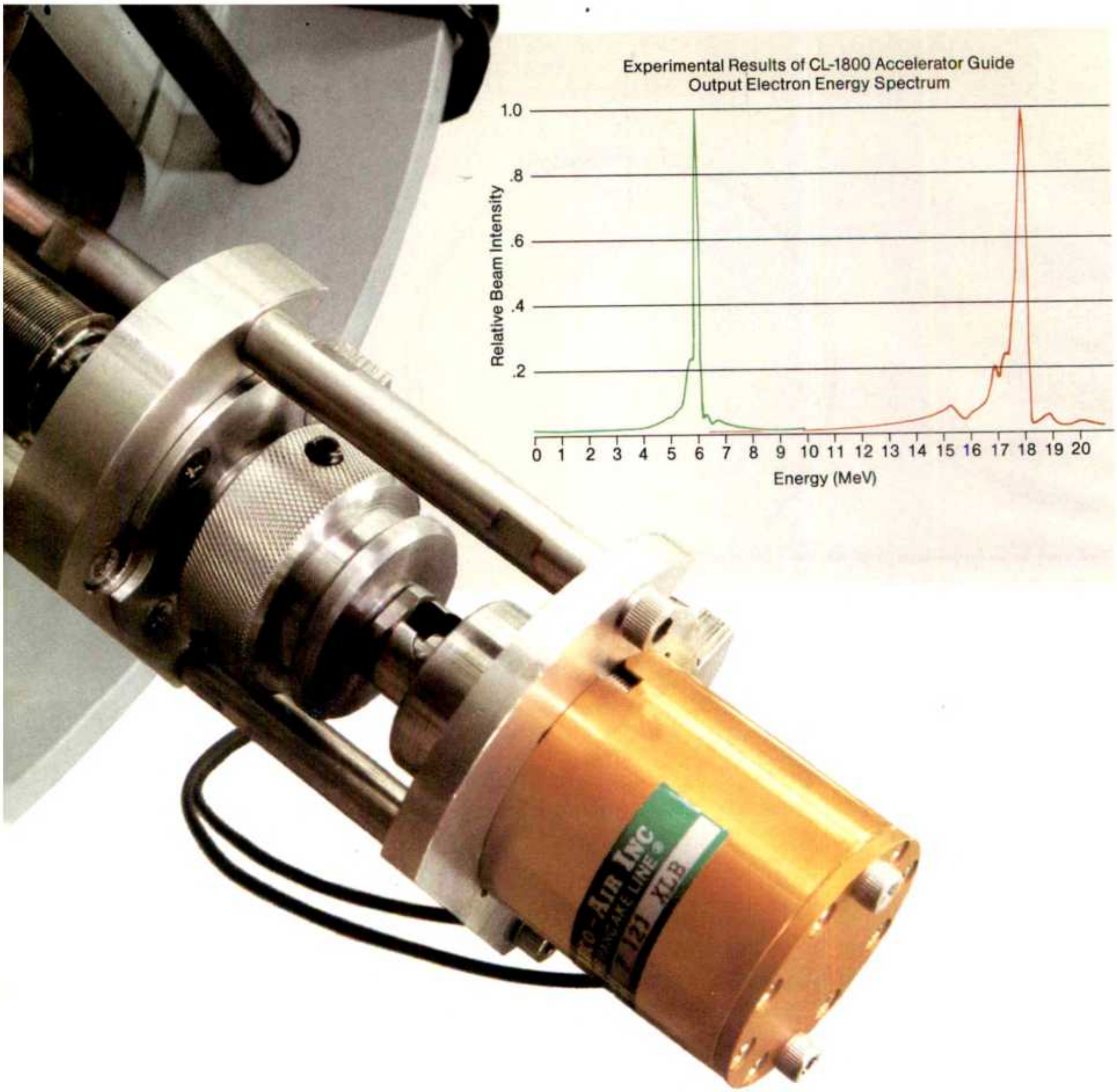

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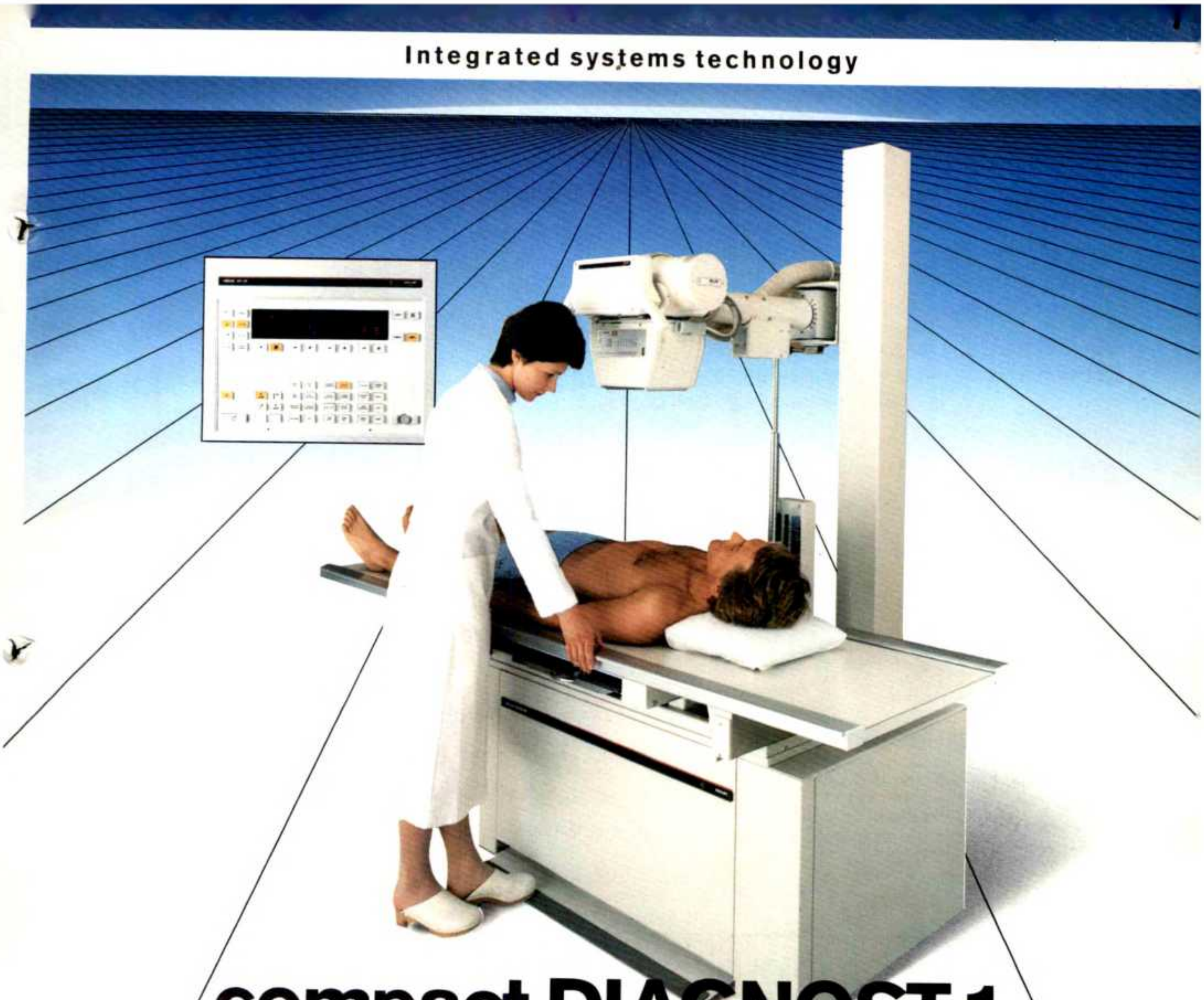

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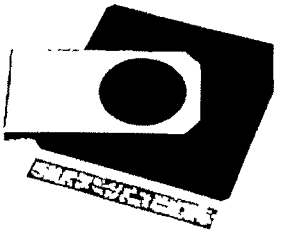

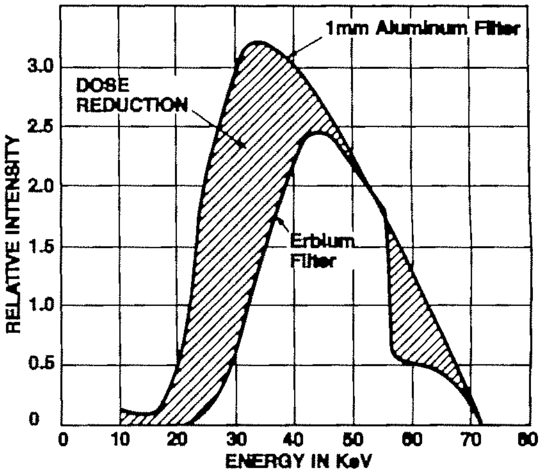

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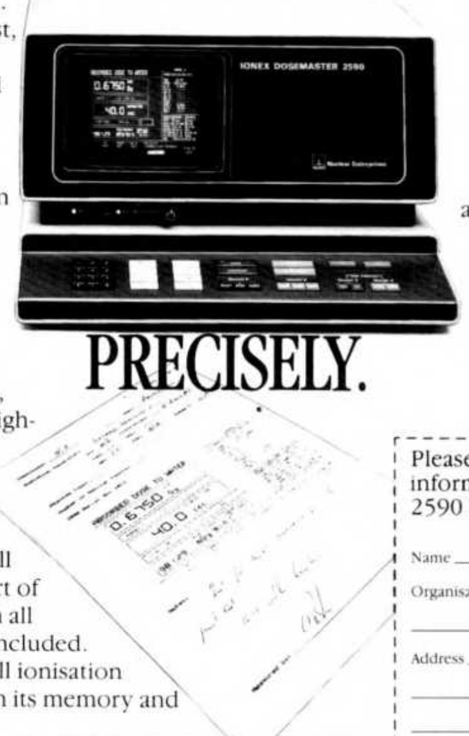

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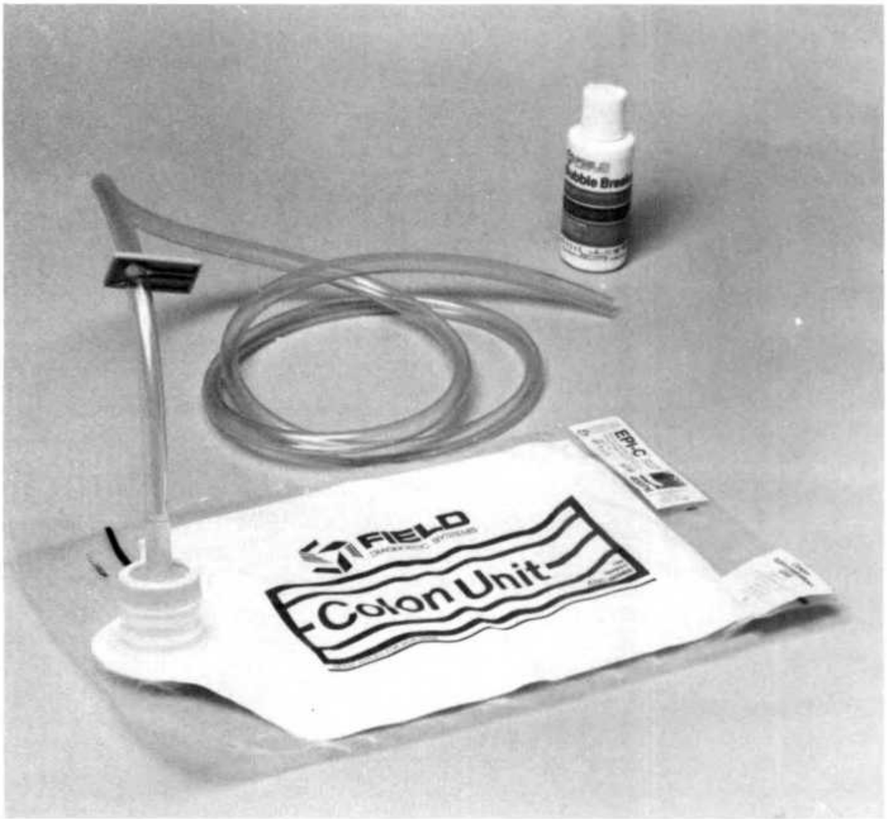

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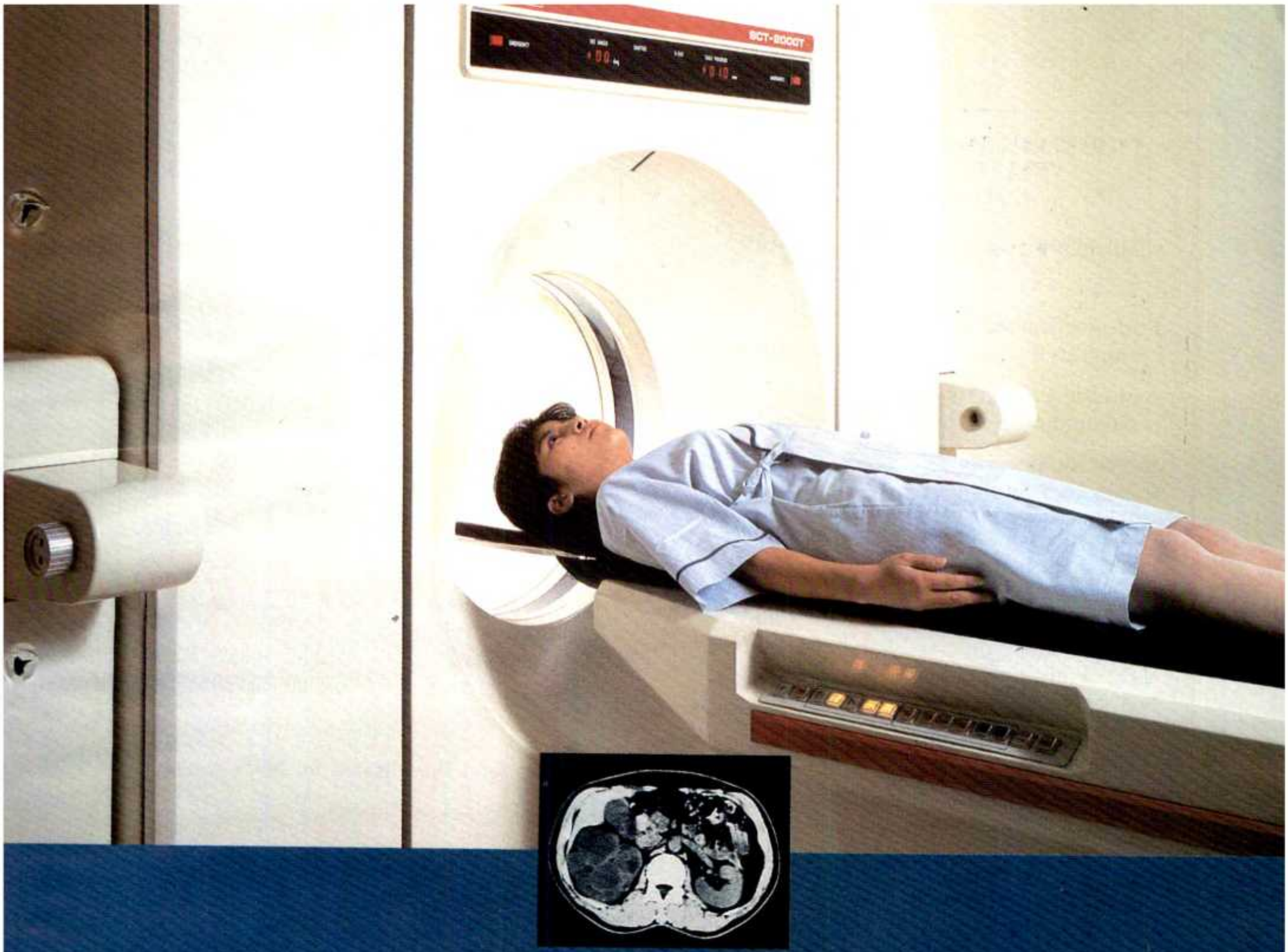

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1986, *The British Journal of Radiology*, 59, 745

VOLUME 59 NUMBER 704 AUGUST 1986

The British Journal of Radiology

Low-attenuation materials and rare-earth screens in radiodiagnosis

Statement by the British Institute of Radiology

The International Commission on Radiological Protection (ICRP) recently (ICRP, 1985) re-emphasised their earlier advocacy (ICRP, 1982) of the more widespread adoption of techniques to reduce the radiation dose to the patient, in particular the use of rare-earth screens and of low-attenuation materials such as carbon fibre to replace the materials currently used in the primary beam.

The British Institute of Radiology wishes to commend these techniques. The old-type tungstate screens are still in widespread use in the United Kingdom and they should be phased out in the near future in favour of rare-earth screens. Although there may be special circumstances when traditional screens are preferred, the image quality obtained with modern rare-earth screens is generally acceptably high, and the combined screen and associated film cost differential is now insignificant. Furthermore, since their use leads to various other savings, such as increased tube life, their benefit is not limited to reducing the radiation detriment of diagnostic radiology. New apparatus including cassettes should be fitted with low-attenuation materials such as carbon fibre material and fibre interfacing in grids. Consideration should be given to incorporating these materials in old machines. This is particularly important for X-ray equipment giving a high dose to the patient, such as fluoroscopy sets.

Although not yet implemented in the UK the EEC Directive 84/466 requires the establishment of criteria of acceptability for radiological installations and that all installations which no longer meet the criteria should be taken out of service or replaced. The advice given here is consistent with this Directive. Furthermore, the application of these methods of dose reduction will conform with the Ionizing Radiations Regulations (1985) Section 33(1) which state that medical exposures should be carried out on apparatus which restricts as far as is reasonably practicable the exposure to ionising radiation of any person undergoing a medical exposure.

REFERENCES

ICRP, 1982 *Protection of the Patient in Diagnostic Radiology*. ICRP Publication 34. Annals of the ICRP, Vol. 9, No. 2/3 (Pergamon Press, Oxford).

ICRP, 1985. *Quantitative Bases for Developing a Unified Index of Harm*. ICRP Publication 45. Annals of the ICRP, Vol. 15, No. 3 (Pergamon Press, Oxford).

Book review

Multiple Primary Cancers in Connecticut and Denmark. NCI Monograph 68, pp. 430+appendix, 1985 (National Institutes of Health, Bethesda, USA)
Copies are available only from: Superintendent of Documents, US Government Printing Office, Washington DC 20402, USA.

This monograph presents detailed analyses of second primary cancers from two long-established population-based cancer registries. The first section of the book provides a welcome update of material from the Connecticut Tumour Registry, covering registrations from 1935 to 1982; in the second part, data from the Danish Cancer Registry, covering the whole of Denmark from 1942 to 1980, have been analysed in a similar way for this joint venture

For each registry, the results for main anatomical systems are presented in chapters by different authors In total, 35 individual sites are considered as both index and second primary sites, with observed and expected numbers of second primaries together with the relative risks displayed in standard tables by time intervals from the index primary. In the Connecticut section additional tables give a further breakdown for long-term survivors (10 years or more) and for treatment (radiotherapy versus other treatment) at appropriate sites. The latter tables will be of interest to the radiotherapist but the fact that allocation to the treatment groups was not random should be taken into account.

Although there is some disparity between the results from the two registries—and the reader is advised to note the differing reporting and recording practices for registration before making comparisons—there is sufficient concordance to identify certain constellations of sites which have emerged with elevated risks, notably those associated with tobacco or alcohol usage, hormone- or diet-related sites and those which might be attributed to treatment of the first cancer. In addition, many other significant associations are identified which will provide a stimulus in the search for further aetiological factors by other epidemiological methods The analyses are based on over 30 000 second primary cancers but more than a further 8000 known cases were excluded for various reasons and it is not clear what effect this loss of information has on the estimated relative risks.

As they stand, the results of the analyses are of clinical importance in indicating areas of high risk where a second, treatable cancer might occur. It is perhaps a matter for regret that chemotherapy could not be addressed in this otherwise commendable volume.

The monograph provides a wealth of information mainly in tabular form but the accompanying text is concise and informative, with discussions weighing the evidence both for possible aetiological and for confounding factors. Reference sections are appended to each chapter and although there is some overlap, the practice is to be commended. Although primarily a reference book, the inquiring clinician or epidemiologist will want a copy to hand.

P. Prior

1986, *The British Journal of Radiology*, 59, 747–748 AUGUST 1986

Editorial

Radiation protection in radiography in the United Kingdom

The book of radiologist martyrs (Holthusen et al, 1959) contains over 300 names. It is not surprising that "radiation protection" in radiodiagnosis for decades had its emphasis on protection of the staff, despite the failure to demonstrate, in a large series, any increased mortality in radiologists currently in the profession (Smith & Doll, 1981) and the knowledge that the patient exposure is thousands of times larger than that of the staff. The new Ionizing Radiation Regulations (Department of Health and Social Security (DHSS), 1985) largely continue in the vein of staff protection. This is not unexpected as they arise from the Health and Safety at Work Act. It seems, however, very unlikely, but for the exception noted below, that their application will result in the staff in diagnostic X-ray departments receiving any less exposure. There are new officers appointed to supervise new documentation and details such as new notices but, in practice, the worker will notice little change. This is an indication of the high standards pertaining in radiation protection of staff in medicine in the United Kingdom in the recent past.

The Regulations do however contain one small section, 33, which reads in part:

> "Equipment used for medical exposure
> 33—(i) Every employer shall ensure that any equipment or apparatus under his control which is used in connection with a medical exposure is of such design or construction, and is so installed and maintained as to be capable of restricting so far as is reasonably practicable the exposure to ionizing radiation of any person who is undergoing a medical exposure to the extent that is compatible with the clinical purpose or research objective in view."

This section will have far reaching consequences. For the first time we have a legal obligation to use only apparatus which gives as small a radiation dose to the patient as possible. Recent developments, and not so recent developments, offer the ability to reduce substantially the dose to the patient. Rare-earth fluorescence was identified early this century and rare-earth screens have been available for some time. Early examples were unsatisfactory because their speed deteriorated rapidly, but current examples have a normal life span and offer, for a given grain size, at least a halving of the radiation dose compared with the old-type tungstate screens (Christensen et al, 1978).

Rare-earth screens cost no more than the tungstate, but in only about half the examinations in the United Kingdom are rare-earth screens used at present (Russell, 1986a). Further large reductions, of around 40%, are available by using low-attenuation materials for components in the primary beam (Hufton & Russell, 1986). If these techniques were in full use a halving of the whole of the man-made radiation exposure would occur (Russell, 1986a) without any detriment to the image. It must not be forgotten that very large reductions in the radiation detriment are also available in the careful use of apparatus. For instance, much of the detriment arises from gonadal irradiation (International Commission on Radiological Protection (ICRP), 1980) and careless coning of the beam to include unnecessarily the gonads gives rise to substantial unneeded exposure (Wall et al, 1980).

The attention of Health Authorities has been particularly drawn to Section 33 of the Regulations (DHSS, 1985), but it is also stated that there "should be no significant resource implications in implementing the Regulations". Certainly there will be some cost. Hospital managers do not want to lay out money without tangible results. Promises for future benefit do not weigh as heavily as those in the short term. On the other hand, the Government has said methods of health promotion are to be encouraged (DHSS, 1981) and radiation protection of the patient in radiodiagnosis as a technique of health promotion is fully costed and highly beneficial (Russell, 1985).

One aspect for which guidance has not been given is the time scale envisaged for implementing the Regulations. Overnight application is impossible, as the manufacturers are not geared up for production. Should the introduction of low-attenuation material be confined to new apparatus or should apparatus in use be modified? Certainly, it is cost-effective to modify apparatus in current use (Russell, 1986b).

How has the position arisen where the population radiation dose in radiodiagnosis is a hundred times that of the whole nuclear fuel cycle (Hughes & Roberts, 1984), but to save a unit of population radiation exposure a hundred or more times more is spent in the nuclear fuel industry? (Russell & Webb, 1985). There is not a scientific illiteracy of those in charge, but it is political pressure which has demanded the spending of large sums on radiation protection in the nuclear power cycle. One of the cardinal principles of radiation protection is "ALARA": "all exposures shall be kept As Low As Reasonably Achievable, economic and social factors being taken into account". This is beautifully worded to allow political demands to be met. National (National Radiation Protection Board (NRPB), 1986) and international (International Atomic Energy Agency (IAEA), 1984) authorities have advised figures which are proper to spend to save a unit of population radiation dose. Radiation protection in radiodiagnosis allows dose reductions costing much less than the sums suggested (Russell, 1986b). The financial argument is indisputable. What is lacking is the "social factor" or public demand to dictate reductions in the radiation from radiodiagnostic exposures. The public feel that "hospital X rays are good for you". This is correct in the sense that the benefits of radiography, in general, outweigh the detriment, but it should not stop us trying to reduce the detriment. Perhaps the offer to halve the whole of the man-made ionising radiation dose (Russell, 1986a) has the simplicity to capture the public imagination. It will not be expensive to take this action. Assuming 70 rooms per million population, £3000 per room and a 10-year life of apparatus, the cost of halving the man-made radiation exposure is £0.02/head of population/year.

The final irony is this. A reduction in patient dose will lead to a corresponding reduction in staff dose. Section 33—(i), designed to reduce patient dose, will have far more effect on staff dose than the rest of the Regulations put together.

J. G. B. RUSSELL

REFERENCES

CHRISTENSEN, E. E., CURRY, T. S. & DOWNEY, J. E., 1978. *An Introduction to the Physics of Diagnostic Radiology* (Lea and Febiger, Philadelphia).

DHSS, 1981 *Care in Action. A Handbook of Policies and Priorities for the Health and Personal Social Services in England* (HM Stationery Office, London).

——1985. *Ionising Radiation Regulations, 1985.* Health circular HC(85)31

HOLTHUSEN, H., MEYER, H & MOLINEUS, W., 1959. *Ehrenbuch der Röntgenologen und Radiologen aller Nationen* (Urban and Schwarzenberg, Munich).

HUFTON, A. P. & RUSSELL, J. G. B., 1986. The use of carbon fibre material in table tops, cassette fronts and grid covers: magnitude of possible dose reduction. *British Journal of Radiology, 59,* 157–163.

HUGHES, J. S. & ROBERTS, G. C., 1984. *The Radiation Exposure of the UK Population—1984 Review.* National Radiological Protection Board (HM Stationery Office, London).

IAEA, 1984. *Costing Transboundary Radiation Exposure* (IAEA, Vienna).

ICRP, 1980. *Recommendations of the ICRP* (Pergamon Press, Oxford)

NRPB, 1986. *Cost Benefit Analysis in the Optimization of Radiological Protection* (HM Stationery Office, London).

RUSSELL, J. G. B., 1985. Cost and effectiveness of methods of radiation protection in X-ray diagnosis. *Clinical Radiology, 36,* 37–40.

—1986a. Assessment of the current use of rare earth screens in the United Kingdom. *British Journal of Radiology, 59,* 630

——1986b. Assessment of priorities when introducing some radiation protection methods in radiodiagnosis. *British Journal of Radiology, 59,* 153–156.

RUSSELL, J. G. B & WEBB, G. A. M., 1985 Spending on radiation protection. *Lancet, i,* 391.

SMITH, P G. & DOLL, R., 1981. Mortality from cancer and all causes among British radiologists. *British Journal of Radiology, 54,* 187–194.

WALL, B. F., FISHER, E. S., SHRIMPTON, P C. & RAE, S., 1980. *Current Levels of General Irradiation from a Selection of Routine Diagnostic X-ray Examinations in Great Britain* (R105) (National Radiation Protection Board, Harwell).

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AUGUST 1986

Doses to patients from routine diagnostic X-ray examinations in England*

By P. C. Shrimpton, Ph.D., B. F. Wall, B.Sc., D. G. Jones, Ph.D., E. S. Fisher, M. C. Hillier, G. M. Kendall, Ph.D. and †R. M. Harrison, Ph.D.

National Radiological Protection Board, Chilton, Didcot, Oxon and †Regional Medical Physics Department, Newcastle General Hospital, Newcastle upon Tyne

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ABSTRACT

A collaborative survey between the National Radiological Protection Board and the Hospital Physicists' Association has been conducted to ascertain current levels of exposure for patients undergoing 10 routine types of X-ray examination in England. The main part of this study consisted of measurements on nearly 3200 patients attending 20 randomly selected English hospitals. The energy imparted to each patient was determined from a measurement of the total exposure–area product for the examination. In addition, thermoluminescent dosemeters were attached to the patient's skin to enable the derivation of doses to the major radiosensitive organs, either directly or using appropriate conversion factors calculated for a mathematical phantom by a Monte Carlo technique. Histograms are presented showing the wide distributions often observed in the doses for each type of examination. Mean values of exposure–area product, energy imparted to the patient, entrance skin dose per film and organ dose are reported, together with coefficients of variation. Comparison of the results with those from similar surveys in the UK and abroad is complicated by inconsistencies in the reporting of such data, but substantial differences are sometimes apparent, particularly for the estimates of organ doses. The present measurements will provide a useful baseline for future measurements and will be used to evaluate the collective dose to the population from medical exposures and the radiation risks from the various radiological procedures.

X-ray examinations are an established tool of medical diagnosis. Their widespread use means that, on the average, a person in Great Britain can expect to experience one every 2 years or so. Patients can undoubtedly derive enormous benefit from these examinations, although the ionising nature of the X rays means that their use is not entirely without risk. For this reason, all exposures to diagnostic X rays need to be both justified and optimised in terms of the associated benefits and risks. One of the requirements for such an exercise is knowledge of the radiation doses and risks involved. Unfortunately, appropriate, detailed data for each type of examination have so far been quite limited. This is due, in part, to the difficulty of assessing the radiation doses to the different organs of a patient undergoing an X-ray examination.

Gonadal doses and the consequential genetic risks of diagnostic radiology in Great Britain were evaluated some years ago by the National Radiological Protection Board (NRPB) (Wall et al, 1981). In a complementary study, consideration is presently being given to the somatic doses and effects. Wall and Shrimpton (1981) have identified two different approaches to the problem of assessing somatic doses to patients undergoing X-ray examinations. The more thorough of these approaches involves the estimation of dose to the major radiosensitive organs, although it is acknowledged that accurate dosimetry may be difficult to achieve in practice. In contrast, the other approach is more pragmatic, being based on a simply derived estimate of the total energy imparted to the patient, regardless of which individual organs are irradiated. Bengtsson and Jensen (1979) have already reported a reasonable correlation between mean energy imparted and radiological risk to the patient.

Both of these, energy-imparted and organ-dose approaches have been adopted in a recently completed national survey of patient doses carried out by the NRPB in collaboration with the Hospital Physicists' Association (HPA). Some preliminary results observed during the course of this survey have already been reported (Shrimpton et al, 1984a; Shrimpton & Wall, 1985; Shrimpton, 1985a). This paper presents a summary for the entire survey of the mean levels of exposure–area product, energy imparted to the patient, entrance skin dose per radiograph and organ doses observed in patients undergoing a selection of common X-ray examinations in England. Further analyses of these data are in progress and will be reported in subsequent publications.

PATIENT DOSE SURVEY

The extent of any dose survey must necessarily be limited and measurements in the present work were confined to 10 routine types of radiological procedure. These were selected on the basis of their likely importance to the collective population dose and fall into two broad categories: six "simple" examinations, commonly involving up to four radiographs, and four "complex" examinations, where more radiographs and possibly fluoroscopy are likely (Shrimpton et al, 1986). These are identified in Table I.

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†Past Chairman of the Diagnostic Radiology Topic Group of the Hospital Physicists' Association.

Measurements were carried out on patients undergoing the selected examinations in accordance with the strategy adopted for assessing somatic risk. We give here a brief outline only of the techniques employed. Full details of the methods and their likely uncertainties will appear elsewhere (Shrimpton et al, 1986). Values of the energy imparted to each patient were determined from the total exposure–area product for the examination, recorded by a Diamentor large-area, transmission ionisation chamber fitted to each X-ray set. According to the calibration previously developed for the Diamentor (Shrimpton et al, 1984b), appropriate energy-imparted conversion factors for each irradiation are primarily dependent on the applied potential and total filtration of the X-ray beam and, to a lesser extent, on the voltage waveform of the generator and the target angle of the X-ray tube. Measurements were also performed with thermoluminescent dosemeters (TLDs) attached to the patient's skin to enable organ doses to be derived. Thyroid, breast and lung doses during the "complex" category of examinations were estimated directly from skin dose measurements over the thyroid (one TLD) and on the front and back of the thorax (two TLDs each). Doses for other organs and examinations were deduced from measurements of entrance skin dose per radiograph or exposure–area product, using conversion factors produced by an extensive series of computer calculations employing Monte Carlo techniques and a mathematical phantom to simulate the irradiation of the patient during the various examinations. Jones and Wall (1985) detail the computational methods used and present tables of factors covering a wide range of radiation qualities for each of 22 X-ray fields.

Measurement techniques were initially developed and refined during a pilot survey of approximately 600 patients at five local hospitals. A further sample of 20 hospitals was then randomly selected as representative of current radiological practice in England. To ensure efficient use of the equipment and time available for the survey, these hospitals were chosen at random from the 306 non-specialised English hospitals returning more than 2×10^5 radiographic workload units for 1980, which between them account for 80% of the total workload for the country. The survey was implemented at each of these hospitals in turn for a period of up to a month, so that between 10 and 20 patients were measured for each of the 10 types of examination at all

TABLE I

THE 10 TYPES OF X-RAY EXAMINATION SELECTED FOR INVESTIGATION AND THE DETAILS OF THE RANDOM SAMPLES OF ADULT PATIENTS COMPRISING THE DOSE MEASUREMENT SURVEY

Examination		Patients		
Type	Comments	Number* (male/female)	Age† years	Weight† kg
"Simple" examinations				
Lumbar spine	Includes lumbosacral joint (LSJ)	365 (185/178)	53 (34)	68 (20)
Chest	Full-size radiographs only	465 (232/232)	55 (35)	65 (20)
Skull	Radiographs of complete skull only	229 (95/133)	51 (43)	65 (20)
Abdomen	Mainly large radiographs of general abdomen	329 (159/167)	58 (33)	68 (22)
Thoracic spine		211 (85/126)	56 (32)	66 (18)
Pelvis	Excludes hip examination	338 (126/211)	62 (27)	65 (20)
"Complex" examinations				
Intravenous urography (IVU)	27% included tomography	357 (224/133)	52 (35)	69 (19)
Barium meal	Excludes follow-through examinations	346 (174/170)	56 (33)	66 (20)
Barium enema	Mainly double-contrast technique	326 (136/190)	59 (29)	65 (20)
Cholecystography	A mixture, including cholangiography	167 (39/128)	50 (34)	68 (21)

*The total numbers of patients include those whose sex was not recorded on the form.

†The ages and weights shown are means, together with coefficients of variation in parentheses (%).

20 hospitals. In this way, an essentially random selection of nearly 3200 patients was monitored for this main part of the survey during 1983 and 1984, covering 97 X-ray tubes in 74 different rooms. A list of all 25 hospitals participating in both phases of the survey is given in the Appendix to this paper

Results

Presentation of data

Each patient record, consisting of results of the measurements and details of the examination and patient, has been stored in a computer to facilitate calculation of organ doses and analysis of the data. In this paper, the survey is summarised in terms of mean values of dose and associated coefficients of variation, together with some histograms to illustrate the often wide ranges observed in the measured and calculated doses for each type of examination. Furthermore, in order that the results should be representative of general practice in England, the data given relate to measurements at the random sample of 20 hospitals. The possibly biased local pilot survey was not included, particularly since some of the differences in mean dose values between it and the main survey were statistically significant. Finally, the doses shown pertain to measurements carried out on all adult patients (age > 15 years); the limited dose data available for the relatively small numbers of children in the survey will be reported elsewhere (Shrimpton et al, 1986). Details of the randomly selected adult patients included for each type of examination are shown in the final three columns of Table I, where the numbers of patients and their mean ages and weights (and coefficients of variation) are indicated. Records of weight were only approximate, being either supplied by the patients themselves or estimated by the radiographers. The ratios of the numbers of male and female patients vary with the type of examination and are in general accordance with those obtained in a previous national survey of X-ray patients (Kendall et al, 1980). The distributions of age and weight of adult patients span factors of about 5.5 and 3, respectively, for each of the selected radiological procedures, with median values being close to the means shown in Table I. The mean patient weights indicated for the examinations are close to the 70 kg mass of the mathematical phantom used in the dose calculations.

More comprehensive results for the survey will be contained in a forthcoming report (Shrimpton et al, 1986).

Diamentor measurements for complete examinations

Measurements with the Diamentor transmission ionisation chamber made during the 10 routine X-ray

TABLE II

Means (with coefficients of variation (%) in parentheses) of measurements on adult patients carried out with the Diamentor transmission ionisation chamber during 10 routine types of X-ray examination

Examination	No. of radiographs	Diamentor measurements for complete examinations			
		No	Screening time, s	Exposure–area product, R cm^2	Energy imparted, mJ
Lumbar spine	3.4 (25)	354	—	1350 (63)	124 (67)
Chest	1.3 (41)	458	—	53 (153)	4.4 (184)
Skull	3.0 (25)	131	—	447 (58)	20.7 (57)
Abdomen	1.4 (40)	322	—	664 (81)	56.7 (90)
Thoracic spine	2.4 (29)	204	—	676 (59)	55.4 (63)
Pelvis	1.1 (27)	324	—	430 (62)	34.8 (65)
IVU	8.2 (30)	357	—	3445 (74)	281 (77)
Barium meal	7.8 (55)	342	193 (61)	2202 (91)	231 (91)
Barium enema	8.5 (30)	325	224 (49)	4817 (67)	501 (70)
Cholecystography	5.0 (51)	164	115* (161)	1094 (104)	90.2 (104)

*Sample size of 16 patients only.

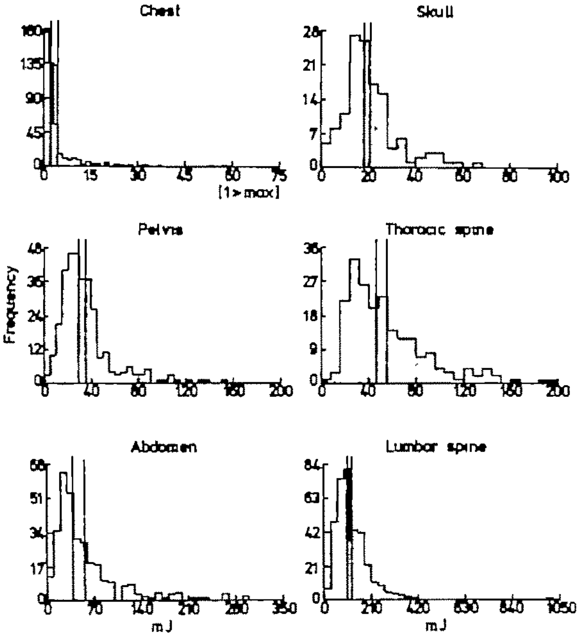

FIG 1.

Histograms of the energy imparted to patients determined for a random sample of adults undergoing "simple" types of X-ray examination in England. Means and medians of distributions are indicated by dotted lines and continuous lines, respectively. The maximum value observed during chest examination of 103 mJ has been omitted from the first histogram

procedures are summarised in Table II. The final two columns of the table give the mean values (and coefficients of variation) of the measurements of total exposure–area product and of the derived estimates of the energy imparted to the patient for each type of examination. Values of exposure–area product are expressed in terms of the non-SI unit R cm^2, consistent with the manufacturer's calibration for the Diamentor. Instrument readings were corrected according to the sensitivity determined for the Diamentor system installed on each X-ray unit (Shrimpton & Wall, 1982). Corresponding values of the air kerma–area product in mGy cm^2 may be obtained from the quoted exposure–area products by multiplying them by 8.69. Figures 1 and 2 show the distributions in energy imparted for "simple" and "complex" procedures, respectively.

The values of fluoroscopic screening time shown in Table II for three of the more complex examinations relate to estimates indicated by the Diamentor. This instrument is able to provide a convenient, but fairly crude, measure of irradiation time, since studies have shown that it includes artefacts associated with the switching on or off of the X-ray beam for radiography, as well as fluoroscopy, during each examination.

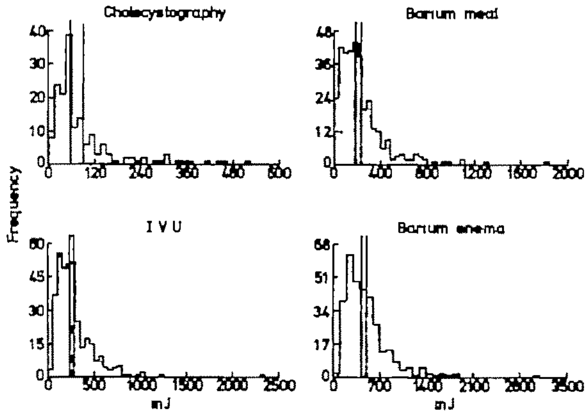

FIG 2

Histograms of the energy imparted to patients determined for a random sample of adults undergoing "complex" types of X-ray examination in England. Means and medians of distributions are indicated by dotted lines and continuous lines, respectively.

Detailed measurements on a small number of patients indicated that the Diamentor could be expected to over-read screening time by approximately 20% during typical barium-meal or -enema examinations. On the other hand, comparison between values of screening time indicated by the Diamentor and by the timer on the X-ray unit itself for groups of patients at several different hospitals, not surprisingly, showed varying degrees of agreement; ratios of timer to Diamentor screening times ranged from 0.68 to 1.00. In view of the uncertainties, therefore, measurements of screening time by the Diamentor are reported without correction.

Table II also shows the mean number of radiographs observed for each type of examination. Numbers for the "complex" procedures involving barium contrast medium include both small-format (70 mm or 100 mm etc.) fluorographic films and conventional full-size radiographs exposed in a screen cassette. Some of these latter radiographs may, in turn, be split into several separate exposures, which are not taken into account in the simple count of radiographs used.

Entrance skin dose measurements per radiograph

Table III summarises measurements carried out for individual radiographs with the radiographic projections commonly used during the six "simple" types of X-ray examination. In the case of the examination of the complete skull, antero-posterior (AP) and postero-anterior (PA) projections are broad classifications which include the various angled projections (*e.g.* Towne's and reverse Towne's, respectively) also used

Mean values of skin dose determined for these routine radiographs are shown in the final column of Table III, with coefficients of variation indicated in brackets. Measurements were made for each individual

TABLE III

MEANS (WITH COEFFICIENTS OF VARIATION (%) IN PARENTHESES) OF ENTRANCE SKIN DOSE MEASUREMENTS ON ADULT PATIENTS DURING COMMON RADIOGRAPHIC PROJECTIONS OF SIX "SIMPLE" TYPES OF X-RAY EXAMINATION

Examination and projection	No. of measurements	Indicated applied potential, kV	Entrance skin dose per radiograph, mGy
Lumbar spine			
AP	428	75.1 (9)	9.19 (65)
Lateral	420	85.2 (10)	22.8 (58)
Lateral LSJ	388	93.7 (10)	38.7 (51)
Chest			
AP	22	60.7 (12)	0.30 (69)
PA	473	68.5 (18)	0.23 (78)
Lateral	84	84.2 (19)	1.46 (120)
Skull			
AP	294	75.3 (10)	4.37 (50)
PA	126	75.8 (8)	4.76 (47)
Lateral	270	67.0 (7)	2.33 (49)
Abdomen, AP	427	74.9 (11)	8.43 (72)
Thoracic spine			
AP	249	76.9 (12)	6.23 (79)
Lateral	252	72.2 (14)	14.0 (66)
Pelvis, AP	359	72.6 (11)	6.57 (60)

radiograph with a dosemeter positioned in contact with the patient's skin and located at the centre of the incident X-ray beam. The doses reported, therefore, include the effects of scattering of the beam by the patient and are expressed in terms of absorbed dose to "ICRU" muscle (International Commission on Radiation Units and Measurements, 1970) in units of mGy. Probably the most frequent of all diagnostic X-ray examinations, a PA projection of the chest, results in a mean entrance skin dose of 0.23 mGy. This is the lowest of those investigated by an order of magnitude or more. Except for the skull, largest doses are associated with X-ray beams projected laterally through the patient, in particular the lateral projection of the lumbosacral joint (LSJ) during the examination of the lumbar spine. Figure 3 shows the distributions of entrance skin dose observed for a sample of the projections. The skewed nature of these histograms is typical of all the projections studied, where coefficients of variation about the observed means are generally between 50% and 80%, as shown in Table III.

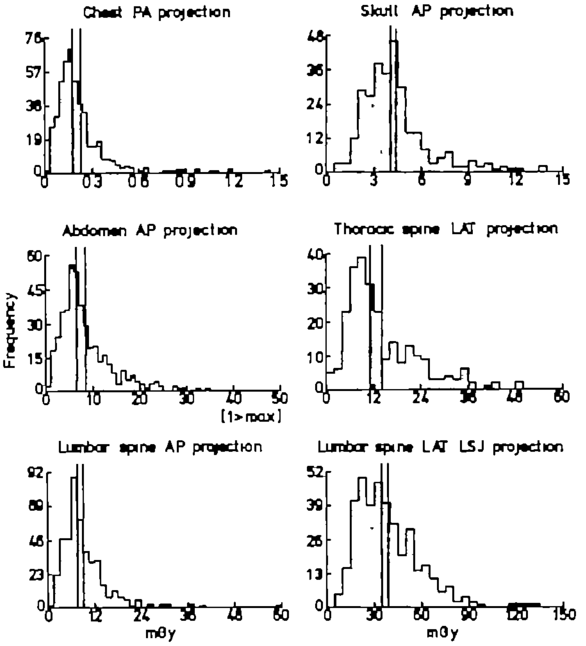

FIG. 3.

Histograms of measurements of entrance skin dose per radiograph during six common X-ray examinations for a random sample of adult patients in England. Means and medians of distributions are indicated by dotted lines and continuous lines, respectively. The maximum value observed during AP projection of the abdomen of 62.4 mGy has been omitted from the third histogram.

Table III also gives the mean values of indicated applied potential used by the radiographers for each of the categories of radiographs studied. These values relate directly to the X-ray generator settings recorded on the patient forms. The spreads in the settings used for each projection are generally quite small; values are distributed reasonably symmetrically about the means shown, with coefficients of variation of 10% or so. The largest variability was found for radiographs of the chest, which were observed in 30 different X-ray rooms, one of which employed a high applied potential (125 kV) technique. During the course of organ-dose and energy-imparted calculations, recorded values of applied potential are corrected in accordance with calibration checks performed on each generator (Shrimpton et al, 1986). Mean values of corrected applied potentials differ from those shown in Table III by no more than 3%, with similar coefficients of variation.

Organ dose estimates for complete examinations

The entrance skin dose measurements for each film have allowed the estimation of doses to all the major

TABLE IV

Means (with coefficients of variation (%) in parentheses) of organ dose estimates for adult patients undergoing six "simple types of X-ray examination

Examination	Organ doses* for complete examinations, mGy										
	Breast	Red bone marrow	Lung	Thyroid	Bone	Skin	Uterus	Ovaries	Testes	Trunk	"Remainder"
Lumbar spine	0.07 (63)	1.41 (62)	0.29 (62)	†	1.56 (57)	2.02 (52)	3.46 (59)	4.33 (58)	0.06 (66)	3.05 (55)	4.47 (57)
Chest	0.09 (289)	0.04 (187)	0.14 (184)	0.02 (276)	0.08 (164)	0.04 (205)	†	†	†	0.07 (186)	0.03 (224)
Skull	†	0.16 (60)	0.01 (64)	0.41 (64)	0.95 (59)	0.34 (60)	†	†	†	0.01 (63)	0.30 (61)
Abdomen	0.03 (103)	0.40 (113)	0.08 (107)	†	0.54 (105)	0.75 (85)	2.89 (98)	2.17 (99)	0.40 (101)	1.53 (92)	3.30 (95)
Thoracic spine	1.33 (89)	0.65 (80)	2.84 (78)	1.45 (91)	1.53 (75)	0.89 (72)	†	†	†	1.32 (76)	0.71 (83)
Pelvis	†	0.18 (76)	†	†	0.32 (74)	0.52 (68)	1.65 (73)	1.21 (73)	4.56 (70)	0.75 (70)	1.55 (72)

*The doses are averages over the specified organ or tissue.
† < 0.01 mGy

radiosensitive organs of the body for each adult patient undergoing the six "simple" types of X-ray examination. This has been achieved using the results of Monte Carlo calculations employing standardised X-ray field sizes and positions and an idealised mathematical phantom representing the patient (Jones & Wall, 1985). Table IV shows the mean values of the total organ doses observed for complete examinations of the "simple" category involving the mean numbers of radiographs given in Table II. As before, values are expressed in terms of dose to ICRU muscle, apart from those for breast, which are calculated assuming a tissue composition of 50% water and 50% fat. Uterus, ovary and testis doses, based on the mathematical phantom calculations, have been estimated for each patient, irrespective of sex. "Trunk" refers to the dose as averaged over the entire trunk of the phantom (excluding the head and legs), whilst the "remainder" dose is the mean of the total doses to the additional five most irradiated radiosensitive organs not otherwise specified in Table IV (International Commission on Radiological Protection (ICRP), 1977). Skin dose is the mean dose over the entire surface of the body as discussed by the ICRP (1978); this is not to be confused with the entrance skin doses per radiograph in Table III. Once again, the total organ doses for particular examinations often span large ranges. A sample of organ dose distributions for individual patients is shown in Fig. 4. These histograms are skewed in a similar way to those for the entrance skin dose measurements from which the organ doses are derived. Coefficients of variation about the mean organ doses are large, rising to over 200% for the small doses associated with the chest examination.

Mean values of organ dose estimates for adult patients undergoing four "complex" types of X-ray examination are given in Table V, together with coefficients of variation; mean numbers of radiographs and screening times of these patients are given in Table II. Examples of the distributions observed for these

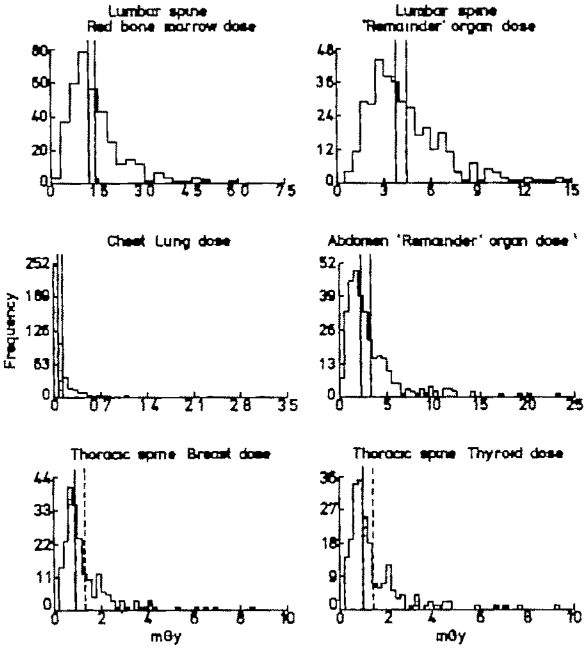

Fig 4.

A selection of histograms of organ dose estimates for a random sample of adult patients undergoing "simple" types of X-ray examination in England. Means and medians of distributions are indicated by dotted lines and continuous lines, respectively.

TABLE V

MEANS (WITH COEFFICIENTS OF VARIATION (%) IN PARENTHESES) OF ORGAN DOSE ESTIMATES FOR ADULT PATIENTS UNDERGOING FOUR "COMPLEX" TYPES OF X-RAY EXAMINATION

Examination	Organ doses* for complete examinations mGy								
	Breast	Red bone marrow	Lung	Thyroid	Bone	Skin	Ovaries†	Testes†	Trunk
IVU	3.91	1.90	4.14	0.39	2.55	3 28	3.58	4 34	6.54
	(209)	(81)	(200)	(175)	(78)	(75)	(95)	(184)	(77)
Barium meal	2.25	2.60	8.65	1.10	3.71	2.05	3.60	0.30	5.12
	(159)	(97)	(126)	(209)	(96)	(90)	(318)	(184)	(90)
Barium enema	0.65	8.17	3 21	0.16	8.76	5 06	16 0	3 35	11.8
	(166)	(77)	(143)	(97)	(76)	(67)	(76)	(189)	(68)
Cholecystography	0.41	0 91	2.28	0.10	1.49	0.93	0.60	0.06	1.99
	(316)	(108)	(203)	(201)	(107)	(104)			(103)

*The doses are averages over the specified organ or tissue.
†Taken from Wall et al (1980).

doses are presented in Fig. 5. Thyroid, breast and lung tissue doses, which were derived directly from TLD measurements, cover very wide ranges, resulting in the large coefficients of variation indicated in Table V. The mean values of ovary and testis dose presented in Table V are those determined previously in a national survey (Wall et al, 1980), together with suitable estimates of gonadal dose for our broad examination classification of "cholecystography" (see Table I). The values of dose shown for all other organs were derived from measurements of exposure–area product using the results of the Monte Carlo calculations and, therefore, possess distributions that are similar in form to that observed for the Diamentor readings. It has not been possible to determine "remainder" organ doses reliably during the "complex" examinations in the detailed way that was possible for "simple" examinations where the X-ray beam geometry is more precisely defined. The mean trunk dose is considered to be the best estimate available for the "remainder" organ dose in the case of "complex" examinations.

DISCUSSION

The present survey provides basic dose data for over 3000 randomly selected adult patients undergoing 10 common types of X-ray examination. The mean numbers of radiographs and mean fluoroscopic screening times indicated in Table II for the sample are in reasonable agreement with corresponding values from a previous British survey (Kendall et al, 1980; Wall et al, 1980). Distributions observed for the various dose quantities are typically skewed, with mean values generally being greater than the corresponding medians or modes and small numbers of patients receiving relatively high doses. Reasons for these spreads in patient doses and inter-hospital variations have been addressed briefly by Shrimpton and Wall (1985) and will be discussed further in a later paper.

Mean values of the energy imparted to patients during each type of examination are summarised in Fig. 6, which also indicates that the minimum and maximum observed for each procedure typically cover a factor of about 50, with the range factor for the chest

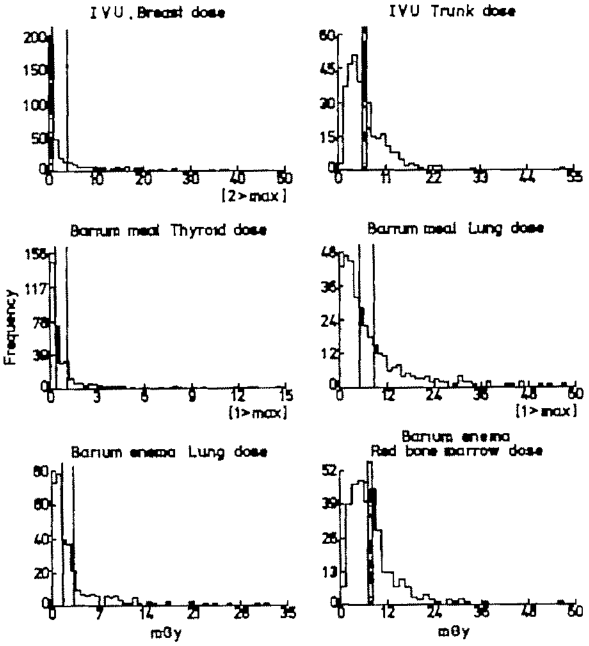

FIG. 5

A selection of histograms of organ dose estimates for a random sample of adult patients undergoing "complex" types of X-ray examination in England. Means and medians of distributions are indicated by dotted lines and continuous lines, respectively. The following maximum observed doses have been omitted from the relevant histograms: breast doses of 93.0 mGy and 59 3 mGy during IVU (first histogram), thyroid dose of 23.8 mGy (third histogram) and lung dose of 106 mGy during barium meal (fourth histogram)

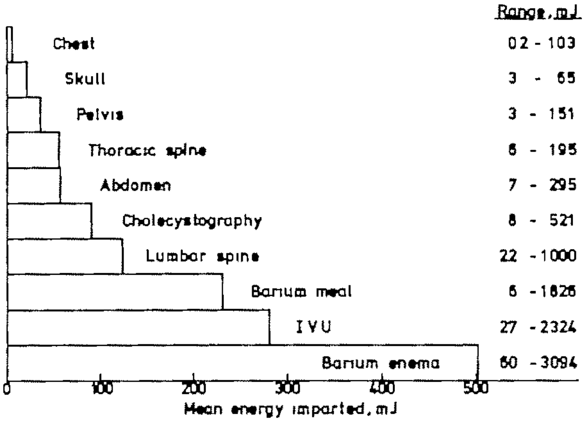

FIG. 6.

Bar chart of the mean values of energy imparted to patients observed for a random sample of adults undergoing 10 routine types of X-ray examination in England, together with the minimum and maximum measurements for each procedure.

examination being over 500. The simultaneous estimation of organ doses and energy imparted made in this survey enables an improved assessment to be made of the relationship between energy imparted and radiological risk to the patient. A preliminary analysis has shown (Shrimpton, 1985b) that, over a range of 100 in dose, there is a reasonable correlation within factors of two or three between mean energy imparted and the quantity effective dose equivalent, as defined by the ICRP (1977). Further analyses will be made using other and possibly more suitable estimates of the risk that can be derived from the basic organ dose data. However, the bar chart in Fig. 6 demonstrates the possible value of a simple measurement of the energy imparted to the patient for indicating the relative risk of examinations covering a wide range of complexity and exposure.

There have been few recent data reported for the exposure–area product or the energy imparted to patients undergoing diagnostic radiology since the pioneering work of Carlsson (1965), who carried out extensive measurements at two Swedish hospitals. Two subsequent surveys in Sweden, one local (Gustafsson, 1979) and one national (Bengtsson et al, 1978), determined mean values of energy imparted that were generally larger than those in the present work. The measurements of exposure–area product in Table II are also less than the results given by Löhr et al (1977) for barium contrast examinations at a West German hospital, although our mean of 4817 R cm^2 for barium enema examination is larger than values published by Bednarek et al (1983) for both single-contrast (2508 R cm^2) and double-contrast (3751 R cm^2) colon studies in the USA However, the values of exposure–area product reported by Beentjes and Broerse (1981), from observations on several types of examination in the Netherlands, are in line with our study.

Results of the present national survey are also in broad agreement with those of a recent extensive regional survey, in which entrance skin doses per film for five types of examination were evaluated by indirect measurement (Harrison et al, 1983). Most notable of the differences in mean dose reported by these surveys is for the lateral LSJ projection of the lumbar spine, where the present value of 38.7 mGy is only 60% of that given by Harrison et al (1983). Comparison of the entrance skin dose data in Table III with the results of other national surveys is often made difficult by the variety of exposure quantities reported, which may or may not include scattering by the patient. However, the levels and variation in patient exposure presently observed are consistent with those determined for 12 types of examination by the Nationwide Evaluation of X-ray Trends (NEXT) surveys conducted annually in the USA (Johnson & Goetz, 1986).

There have been few comprehensive publications of organ dose data for diagnostic radiological procedures, which is probably a reflection of the difficulties of achieving suitable dose estimates for many of the organs. The most recently published report from the United Nations Scientific Committee on the Effects of Atomic Radiations (UNSCEAR, 1982) cites numerous references for absorbed doses in various tissues reported from different countries, and notes both the inconsistencies in presentation of the data and also the very large differences in any commonly expressed entries. Comparison of our organ dose data with results from similar surveys, such as that carried out in Sweden (Bengtsson et al, 1978), indeed indicates large discrepancies for certain organs and examinations, which must be due at least in part to the differences in dosimetric techniques used. Values of mean red bone marrow dose given in Tables IV and V may be compared with those determined by the only other national survey of radiological hazards to patients in Great Britain (Adrian Committee, 1966). Doses measured over 20 years ago by that survey for our 10 selected procedures are about three times larger than the present estimates, with the factor varying between unity in the case of barium enemas and 7.5 for pelvis examinations. Whilst there are some differences between the mean entrance skin doses, numbers of radiographs and screening times observed for corresponding examinations by these surveys, many apparent changes in the mean marrow doses are probably the result of the very different methods of measurement used.

Despite the present use of sophisticated Monte Carlo techniques to overcome the basic inability to measure doses directly for most of the organs during diagnostic radiological procedures, one must not overlook the uncertainties that may exist for many of the doses derived for individual patients. The high precision often associated with TLD measurements and computed organ dose conversion factors should not serve to conceal the possibility of errors arising from incorrect positioning of a TLD on the patient's skin or from differences in anatomy and X-ray field geometry between the mathematical simulation and a patient undergoing an examination. Uncertainties are also likely for the estimates of mean dose to the thyroid, breast and lung of a patient having one of the "complex" category of examinations, where a small number of skin dose measurements is made overlying these organs. Such errors are difficult to quantify in practice for individuals, although efforts were made to minimise them through the careful choice of the routine measurement techniques and models used. However, these uncertainties are likely to be of less importance from the point of view of large numbers of measurements on heterogeneous populations of patients examined at many X-ray departments and having ranges of physique and clinical requirements.

The mean values of organ dose estimates presented for each type of examination may, therefore, be considered to be representative of the doses received by an average adult patient undergoing that examination in England. These data will be used to reassess the collective dose to the population arising from diagnostic X-rays and also to evaluate the radiation risks from the various radiological procedures. Furthermore, it is hoped that the values of exposure–area product, energy imparted, entrance skin dose per radiograph and organ doses reported for the survey will represent useful baselines for any future measurements.

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The authors are pleased to acknowledge the co-operation of both patients and staff at all the X-ray departments participating in the survey. In particular, we are indebted to the many hard-working radiographers who performed the patient-dose measurements with enthusiasm and diligence, to hospital physicists for assisting with local arrangements and to members of the Diagnostic Radiology and Radiation Protection Topic Groups of the Hospital Physicists' Association for their comments We also wish to thank Mr S. F Barry for statistical assistance and to record the support and encouragement of the late Dr J. A. Reissland during the initial stages of the survey

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REFERENCES

ADRIAN COMMITTEE, 1966. *Final Report of the Adrian Committee on Radiological Hazards to Patients* (HMSO, London)

BEDNAREK, D. R, RUDIN, S., WONG, R & ANDRES, M. L., 1983. Reduction of fluoroscopic exposure for the air-contrast barium enema. *British Journal of Radiology, 56,* 823–828

BEENTJES, L B & BROERSE, J. J., 1981 Dose from diagnostic radiology in the Netherlands: implications for population dose. In *Proceedings of Seminar on Patient Exposure to Radiation in Medical X-ray Diagnosis, Munich-Neuherberg, April 1981.* Ed. by G. Drexler, H Eriskat & H. Schibilla, (CEC, Luxembourg), pp. 87–100.

BENGTSSON, G., BLOMGREN, P -G , BERGMAN, K. & ÅBERG, L., 1978 Patient exposures and radiation risks in Swedish diagnostic radiology. *Acta Radiologica Oncology, 17,* 81–105

BENGTSSON, L G. & JENSEN, M., 1979. Significance of photon attenuation for the choice of quantities in X-ray protection. In *Proceedings of Seminar on Application of the Dose Limitation System for Radiation Protection Practical Implications, Vienna, March 1979.* IAEA-SR-36 (IAEA, Vienna)

CARLSSON, C., 1965. Integral absorbed doses in roentgen diagnostic procedures II Measurement of integral doses in two roentgen diagnostic departments. *Acta Radiologica Therapy, Physics, Biology, 3,* 384–408.

GUSTAFSSON, M., 1979. Energy imparted in roentgen diagnostic procedures. Results of two surveys during the periods 1958–1960 and 1974–1976 related to technical modifications. *Acta Radiologica Diagnosis, 20,* 123–144.

HARRISON, R M., CLAYTON, C. B., DAY, M. J., OWEN, J. P. & YORK, M. F., 1983. A survey of radiation doses to patients in five common diagnostic examinations *British Journal of Radiology, 56,* 383–395.

ICRP, 1977. *Recommendations of the International Commission on Radiological Protection.* Publication 26, Annals of the ICRP, Vol 1(3) (Pergamon Press, Oxford)

——1978. *Statement from the 1978 Stockholm Meeting of the International Commission on Radiological Protection.* Annals of the ICRP, Vol. 2(1) (Pergamon Press, Oxford)

ICRU, 1970. *Radiation Dosimetry X-rays Generated at Potentials of 5 to 150 kV.* ICRU Report 17 (ICRU Publications, PO Box 30165, Washington DC 20014, USA).

JOHNSON, D W. & GOETZ, W A, 1986. Patient exposure trends in medical and dental radiography *Health Physics, 50,* 107–116.

JONES, D G. & WALL, B. F, 1985. *Organ Doses from Medical X-ray Examinations Calculated Using Monte Carlo Techniques* NRPB Report NRPB-R186 (HMSO, London).

KENDALL, G M, DARBY, S C, HARRIES, S. V & RAE, S, 1980. *A Frequency Survey of Radiological Examinations Carried Out in National Health Service Hospitals in Great Britain in 1977 for Diagnostic Purposes.* NRPB: Report NRPB R-104 (HMSO, London).

LOHR, H., VON, VOGEL, H., REINHART, J. & JANTZEN, R., 1977. Differences of X-ray exposure between roentgen examen with a conventional roentgen-screen-system and with an image-intensifier-television-unit. *Fortschritte auf dem Gebiete der Roentgenstrahlen und der Nuklearmedizin, 126,* 482–488.

SHRIMPTON, P. C., 1985a. Calculation of patient skin dose from diagnostic X-ray procedures Letter to the Editor, *British Journal of Radiology, 58,* 483–485.

——1985b. Energy imparted as a measure of radiological hazard to patients from X-ray examinations. *Medical and Biological Engineering and Computing, 23* (Suppl. Part 2), 1135–1136.

SHRIMPTON, P. C. & WALL, B. F, 1982 An evaluation of the Diamentor transmission ionisation chamber in indicating exposure–area product (R cm^2) during diagnostic radiological examinations. *Physics in Medicine and Biology, 27,* 871–878

——1985 Preliminary observations on the relationship between patient exposure and imaging techniques in a sample of British hospitals. *British Journal of Radiology,* Suppl 18: *Criteria and Methods for Quality Assurance in Medical X-ray Diagnosis,* 127–129.

SHRIMPTON, P C., WALL, B. F., FISHER, E S., JONES, D G. & HARRISON, R. M., 1984a NRPB/HPA survey of somatic doses to patients from X-ray examinations. Abstract of poster presented at HPA 40th Anniversary Conference, Newcastle, September 1983. *Physics in Medicine and Biology*, *29*, 171.

SHRIMPTON, P. C., WALL, B. F., JONES, D. G. & FISHER, E. S., 1984b. The measurement of energy imparted to patients during diagnostic X-ray examinations using the Diamentor exposure-area product meter. *Physics in Medicine and Biology*, *29*, 1199–1208.

SHRIMPTON, P. C., WALL, B. F., JONES, D. G., FISHER, E. S., HILLIER, M. C., KENDALL, G. M. & HARRISON, R. M., 1986. *A National Survey of Doses to Patients Undergoing a Selection of Routine X-ray Examinations in English Hospitals.* NRPB Report (to be published).

UNSCEAR, 1982. *Ionising Radiation: Sources and Biological Effects.* UNSCEAR Report (United Nations, New York).

WALL, B. F., FISHER, E. S., SHRIMPTON, P. C. & RAE, S., 1980. *Current Levels of Gonadal Irradiation from a Selection of Routine Diagnostic X-ray Examinations in Great Britain.* NRPB Report NRPB R-105 (HMSO, London).

WALL, B. F., RAE, S., DARBY, S. C. & KENDALL, G. M., 1981. A reappraisal of the genetic consequences of diagnostic radiology in Great Britain. *British Journal of Radiology*, *54*, 719–730.

WALL, B. F. & SHRIMPTON, P. C., 1981. Deliberations on a suitable quantity and technique for assessing the somatic risk for diagnostic radiology. In *Proceedings of Seminar on Patient Exposure to Radiation in Medical X-ray Diagnosis, Munich-Neuherberg, April 1981.* Ed. by G. Drexler, H. Eriskat & H. Schibilla (CEC, Luxemboug) pp. 413–425.

APPENDIX

HOSPITALS PARTICIPATING IN THE NRPB/HPA DIAGNOSTIC RADIOLOGY SOMATIC DOSE SURVEY

Phase I: Pilot survey of five local hospitals
- Hackney Hospital, London
- Princess Margaret Hospital, Swindon
- St Bartholomew's Hospital, London
- Weymouth and District Hospital
- Whittington Hospital, London

Phase II: Main sample of 20 randomly selected hospitals
- Birch Hill Hospital, Rochdale
- Charing Cross Hospital, Fulham
- Dudley Road Hospital, Birmingham
- Epsom District Hospital
- General Hospital, Hartlepool
- Gloucestershire Royal Hospital, Gloucester
- Good Hope Hospital, Sutton Coldfield
- Ipswich Hospital (Heath Road Wing)
- Leicester General Hospital
- Mayday Hospital, Thornton Heath
- Nottingham City Hospital
- Orpington Hospital
- Pinderfields General Hospital, Wakefield
- Prince of Wales' General Hospital, Haringey
- Royal Cornwall Hospital (Treliske), Truro
- Royal Infirmary, Halifax
- Royal Victoria Hospital, Boscombe
- Royal Victoria Infirmary, Newcastle upon Tyne
- Scarborough Hospital
- St James' Hospital, Balham

1986, *The British Journal of Radiology*, 59, 759–764

Ultrasonography of the normal adrenal glands: a study using linear-array real-time equipment

By Franco Zappasodi, M.D., *Lorenzo E. Derchi, M.D. and †Giorgio Rizzatto, M.D.

Servizio di Radiologia, Ospedale di Forlì, *Istituto di Radiologia, Cattedra B, Università di Genova and †Servizio di Radiologia, Ospedale di Gonzia, Italy

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ABSTRACT

The adrenal glands were evaluated in 70 normal volunteers using linear-array real-time ultrasonography. All the scanning approaches described for manual B-scanning were used and, on the left side, longitudinal scans along the axillary lines were also performed The right adrenal gland was imaged in 68 of the 70 volunteers and the left gland in 63. The dynamic capabilities of real-time equipment were of great help for proper localisation and identification of the glands. Changes in the scanning plane demonstrated variations in the adrenal morphology, because different portions of the gland were encountered by the scanning beam.

Identification of the normal adrenal glands by ultrasonography has been shown to be possible using manual B-scan equipment and following a variety of scanning techniques which have been developed expressly for this purpose (Sample, 1977, 1978; Yeh, 1980). They are based on a two-step procedure: first, visualisation of the different structures surrounding the adrenal region; then identification, along specific scan planes, of the adrenal glands.

Using such scanning techniques, identification rates of the normal adrenal glands by ultrasonography vary from 85%, with no differences between the right and left sides (Sample, 1977), to 91% on the right and 44% on the left (Yeh, 1980). The diagnostic accuracy of this method in the evaluation of patients with adrenal gland diseases has been reported to reach 93% (Sample & Sarti, 1978; Yeh et al, 1978a,b).

However, to image the adrenal glands by ultrasonography is both difficult and time-consuming (Sample & Sarti, 1978), and there are no other reports in the literature of such an effective use of ultrasonography in this field (Abrams et al, 1982).

Due to ease of operation, short examination time and good picture quality, real-time ultrasonography has become the method of choice in evaluating the abdomen by ultrasound and the same results achieved by manual B-scanning have been reported by this technique in a large variety of abdominal conditions (Bartrum & Crow, 1979; Sanders, 1979, Lee et al, 1981; Cooperberg, 1983; Hunter & Haber, 1983).

In this paper we present the scanning techniques we have used and the results achieved by high-resolution linear-array real-time ultrasonography in the evaluation of normal adrenal glands.

SUBJECTS AND METHODS

Seventy normal volunteers (age range 22–57 years) were examined by ultrasonography using a variety of commercially available linear-array real-time equipment with 3.5 MHz electronically focused transducers. Subjects were divided into three groups according to their body habitus: 20 ectomorphs, 26 endomorphs and 24 mesomorphs. In all cases, identification of the adrenal glands was attempted using all the different scanning approaches that have been described for manual B-scanners (Sample, 1977, 1978; Yeh, 1980). On the left side, an additional scanning technique was used: with the patient supine or with the left flank slightly elevated, longitudinal or oblique sections along the axillary lines were performed. The transducer was placed in the intercostal spaces and, using the spleen as an acoustic window, the scan plane was angled towards the adrenal region (Fig. 1).

The suprarenal regions were identified by delineation of all the different structures which surround them: on the right, the liver, the right diaphragmatic crus, the inferior vena cava and the upper pole of the kidney; on the left, the spleen, the left diaphragmatic crus, the aorta and the upper pole of the kidney. The criterion used to classify each examination as positive was visualisation of the adrenal glands.

In most cases the study was performed during suspended normal respiration; in subjects with low-lying pulmonary bases better results could be obtained during forced expiration, while in those with kidneys positioned high, scanning during forced inspiration was preferred. In some cases studies of the left adrenal were performed with the subject standing, slightly flexed towards the right side, with the left arm raised.

RESULTS

The adrenal gland was identified, on the right side, in 68 of the 70 subjects; on the left, it was seen in 63 cases. The results of our study following the division of volunteers in three groups according to their body habitus are presented in Table I.

Address for correspondence and reprints. Dr Derchi, Istituto di Radiologia, Università di Genova, Viale Benedetto XV, 16132, Genova, Italy.

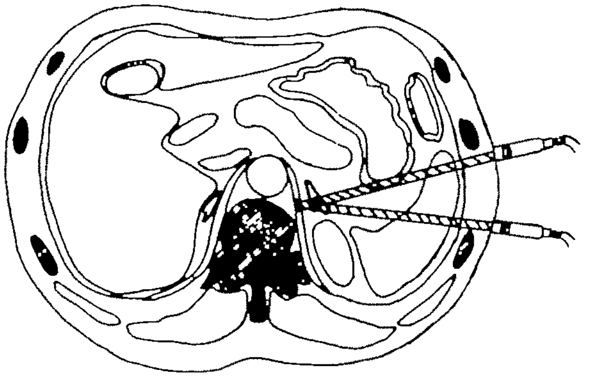


FIG 1.

Schematic drawing illustrating the scan plane used for longitudinal imaging of the left adrenal gland. The transducer array is placed in the intercostal spaces, along the axillary lines, and the beam is directed medially, towards the adrenal; the spleen acts as an acoustic window to the gland. While observing the image on the screen, small changes in orientation of the beam are usually needed in order to obtain the best image in each patient.

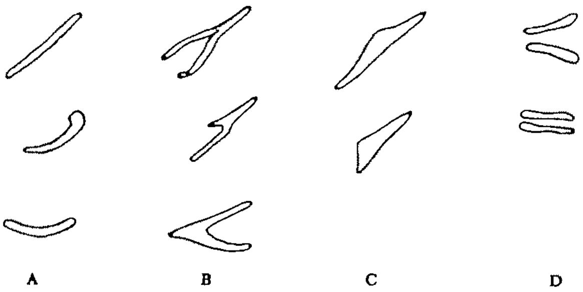


FIG. 2

Drawing of the most common shapes of the adrenal gland we observed. (A) Single-line appearance; this linear structure may present as a straight or curved line or with a "comma-like" pattern. (B) Inverted Y or inverted V image; the angle formed by the wings of the gland is directed cranially (longitudinal scans) or medially (transverse images). In some cases, the wings were not of the same length. (C) The triangular pattern was observed when only the body of the gland was seen, or when the wings were not well developed. (D) Double-line appearance, either parallel or diverging lines were observed. This image was seen when, on longitudinal scans, both wings were within the section plane.

The right adrenal gland could not be identified in two obese subjects, both with fatty livers, and even the structures of the adrenal region were not delineated. On the left, identification of the gland was not achieved in four obese volunteers: in two, structures of the adrenal region could not be delineated, in one, the kidney was positioned high, beneath the costal margin, and in one there was a large quantity of perirenal and pararenal fat and the adrenal gland could not be resolved. The left adrenal gland was not identified in two further subjects with normal body habitus and in one thin volunteer. In these three subjects there was a small spleen, providing no acoustic window, and reverberation artefacts arising from the lung base obscured the adrenal area.

The gland presented as different shapes according to the different portions of it encountered by the scanning beam; the most common shapes we observed are summarised in Fig. 2.

Right adrenal gland

Transverse scans obtained along the axillary lines. The adrenal gland was similar to an inverted Y or V when both its wings were within the scan plane, to a straight or curved line when only one wing was seen, or to a triangle when the lateral wings were not well developed (Fig. 3). Different shapes of the gland were observed while moving the scan plane in a cranio-caudal direction; the most cranial part of the gland, the body, always had a linear shape while, more caudally, the presence of the wings gave rise to the well known, inverted Y appearance of the gland.

TABLE I

IDENTIFICATION OF THE ADRENAL GLANDS

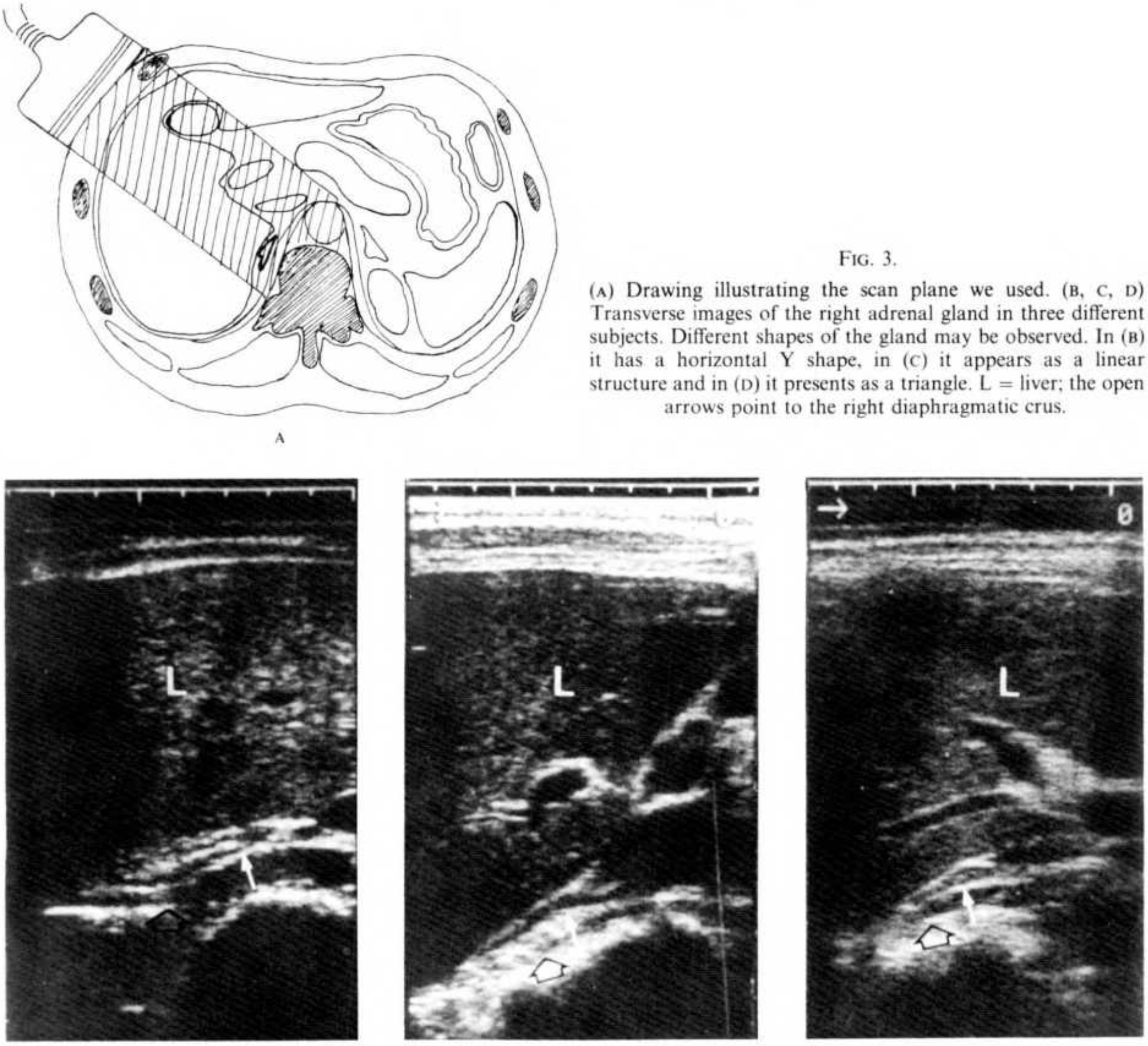
Body habitus (No. of subjects)	Sonographic identification of	
	right gland	left gland
Endomorphs (26)	24	22
Ectomorphs (20)	20	19
Mesomorphs (24)	24	22

Longitudinal scans obtained along the axillary lines. The ultrasonic beam was directed in a latero-medial direction in order to visualise, first of all, the inferior vena cava; then it was angled posteriorly, towards the adrenal region. The right diaphragmatic crus could be observed and, anterior to it, the gland could be seen. It appeared as a single line when the plane was passing through the body and/or only one wing, or as a double-line structure when the section was passing through both wings (Fig. 4).

Anterior longitudinal scans. With the subject in the supine position, using longitudinal scans passing through the inferior vena cava and the scan plane slightly angled in a medio-lateral direction, the gland could be seen posteriorly to the vessel, approximately at the level of the right portal branch. It had a horizontal Y or V shape, with the angle formed by its wings pointing superiorly, or it appeared as a single line or as a triangle (Fig. 5).

Left adrenal gland

Transverse scans. On anterior transverse scans of the epigastrium, in our series the left adrenal gland could be imaged posterior to the tail of the pancreas, only in thin subjects. The gland presented as a single-line structure which probably corresponded to the lateral wing



A

B

C

D

FIG. 3.

(A) Drawing illustrating the scan plane we used. (B, C, D) Transverse images of the right adrenal gland in three different subjects. Different shapes of the gland may be observed. In (B) it has a horizontal Y shape, in (C) it appears as a linear structure and in (D) it presents as a triangle. L = liver; the open arrows point to the right diaphragmatic crus.

Transverse sections through the left flank, using the spleen as an acoustic window to the adrenal region, did not give the same good results reported using B-scanners (Yeh, 1980). In this series, the left adrenal gland could only rarely be seen on these sections, with an inverted Y or inverted V shape.

Longitudinal scans along the axillary lines. Longitudinal scans along the axillary lines were the best approach to the left adrenal gland. In most cases, the gland appeared as a single-line structure between the diaphragmatic crus and the medial aspect of the upper pole of the kidney, often extending cranially to the kidney itself. This structure may be related to the body and/or the medial wing of the gland. In some cases, by gently sweeping the transducer in a medio-lateral direction, it was possible to see this image become a double-line structure, due to passage of the beam through both wings of the gland (Fig. 6).

Coronal scans of the right and left kidneys

Identification of the adrenal glands following the coronal scans of the kidneys proposed by Sample (1977, 1978) has not been possible. Using linear-array equipment, cranial angling of the ultrasonic beam through the upper pole of the kidney was not feasible due to the relatively large dimensions of the transducer.

The only dimension of the adrenal gland that could be measured reliably in all subjects was thickness (maximum value at the body, 0.56 cm; maximum value at the wings, 0.28 cm).

The cranio-caudal (length) and lateral (width) diameters of the adrenals varied widely, depending on

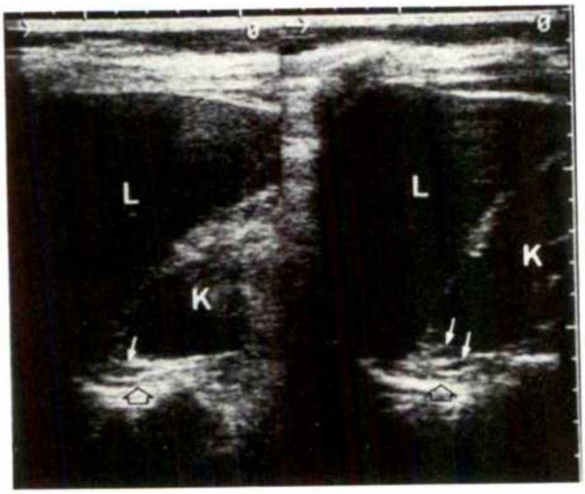


FIG. 4.

Longitudinal sections of the right adrenal gland obtained along the anterior axillary line in the same subject. The image on the left shows the adrenal gland (arrow) with a linear shape, anterior to the diaphragmatic crus (open arrow). The scan on the right is a slightly more lateral image passing through the adrenal wings: the gland (arrows) appears as a double-line structure. L = liver; K = right kidney.

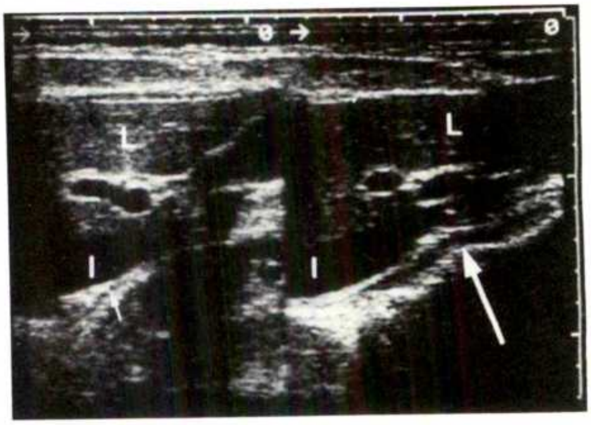


FIG. 5.

Anterior longitudinal scans passing through the inferior vena cava in the same subject. On the right, the diaphragmatic crus may be identified as an elongated and thick structure (long arrow) posterior to the inferior vena cava. On the left, a slightly more lateral section allows identification of the gland, which appears as a thin linear image (small arrow). L = liver; I = inferior vena cava.

the portions of the organ contained within the same scan plane. However, the maximum length within the same scan plane measured in this series was 4.2 cm, while the maximum width (body + wing) was 3.5 cm.

The structure of the gland was hypoechoic, with small echoes of the same, or slightly inferior, echogenicity as the adjacent diaphragmatic crus. In some cases, a few higher level echoes could be noted in the centre of the gland, arranged along a thin line, suggesting a three-layered echo pattern (Fig. 7). Based on observations in neonatal adrenal glands, these three lines may possibly be related to the medullary and cortical portions of the gland (Oppenheimer et al, 1983).

On the right side, on some transverse images, the adrenal gland had an asymmetric X shape, with the long branches pointing postero-laterally and the short limbs directed antero-medially towards the inferior vena cava. The long branches of the X may be related to the wings of the gland and one of the short limbs may be due to the body of the organ. The remaining branch, which seemed to extend more medially to reach the postero-lateral wall of the inferior vena cava, may be interpreted as the central vein of the right adrenal gland. This finding may also be observed on computed tomographic (CT) images, and relates to the anatomical position and the dimensions of the central vein of the gland (Mitty & Yeh, 1982) (Fig. 8).

DISCUSSION

Identification of structures of small size and of complicated three-dimensional configuration is easier using real-time equipment than by manual B-scanners. The dynamic capability of these machines makes identification of the most suitable scan plane easier, since the structure itself may be continuously visualised while changing the scan plane with small movements of the real-time probe. When applied to the study of the adrenal, real-time ultrasonography makes easier differentiation of the gland from the many structures which surround it (for example, the diaphragmatic crura may be identified by following their course cranially, to join the diaphragm, or caudally, towards the insertion on the spine) and greatly facilitates identification of the best longitudinal, transverse, or oblique scanning plane for each patient. Furthermore, only about 15 min are needed for evaluation of both glands. However, it must be noted that the same technical criteria used with manual B-scanning, *i.e.* careful and meticulous choice of the best scan plane, identification of all structures which surround the gland and use of multiple approaches in order to image the various portions of the gland from different angles, must also be adhered to with real-time machines.

On the right side, the right lobe of the liver gives a large acoustic window to the gland, which may be analysed from different points of view and then have all its portions imaged. On the left, the ultrasound approach to examine the gland is more limited and imaging of the organ may not be complete. In most cases it is limited to visualisation of the body and medial wing.

Using manual B-scanners, Sample (1977, 1978) and Yeh (1980) reported that small, tortuous vessels such as the splenic and renal arteries and veins may be confused with a normal adrenal gland, and the oesophago-gastric

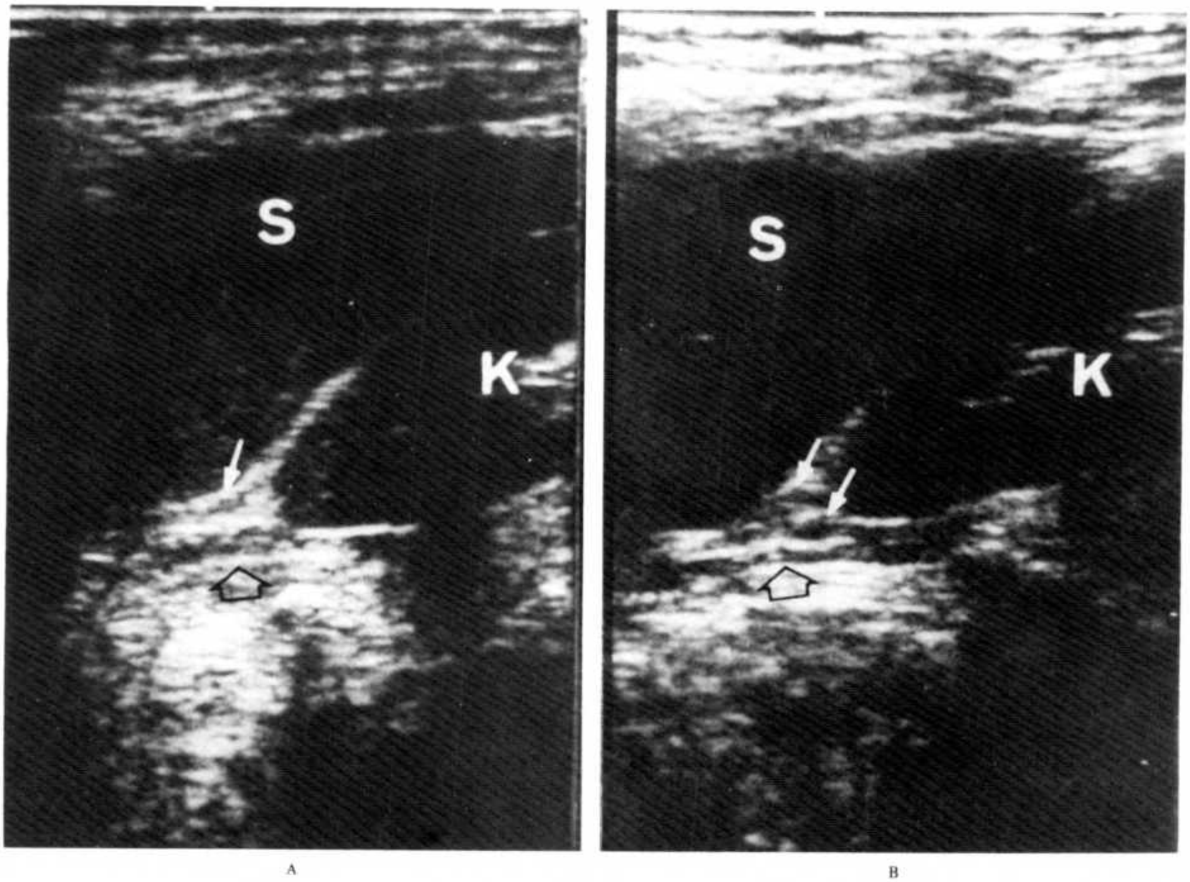


FIG. 6.

Longitudinal scans of the left adrenal obtained along the axillary line in the same subject. In (A) only the body and the medial wing are within the scan plane and the gland (arrow) presents as a single line. In (B), a more lateral section, both wings (arrows) are within the scan plane and an inverted V shape is seen. S = spleen; K = left kidney; the open arrow points to the left diaphragmatic crus.

junction and the second and fourth portions of the duodenum may be misinterpreted as small adrenal masses. Using real-time scanning, such pitfalls seem easier to avoid, due to the dynamic identification of different suprarenal structures. Possible sources of misinterpretation more difficult to avoid are the presence of small lymph nodes in the crural region, or of nodular thickening of the diaphragmatic crura. The second of these pitfalls may be avoided by scanning in different degrees of respiration, since this will alter crural thickness or nodular thickening may disappear. Furthermore, it will be possible to identify the continuity of the nodules with the normal diaphragmatic crus.

Recently Günter et al (1984) have published a paper about real-time ultrasonography of the adrenal gland and, using a mechanical sector scanner, have been able to image the normal gland in only one of 60 subjects. We cannot fully explain the reason for this discrepancy with our results. One explanation may be the use of different types of equipment: in sector images, there is a decrease in line density which is directly related to depth, and this may cause a significant loss of resolution in the analysis of small and deeply located structures, such as the adrenal gland.

Ultrasonography is not currently considered to be the imaging method of choice in the evaluation of patients with suspected adrenal disease. Better results, in terms of both sensitivity and specificity, have been reported using CT in this field (Abrams et al, 1982). However, comparison studies have been based mainly on manual B-scan ultrasonography, and real-time scanning is better at demonstrating the adrenal than B-scan ultrasound. Higher accuracy in the detection of pathological changes affecting the adrenal may be achievable by using real-time ultrasound. Prospective studies which compare the diagnostic accuracy of CT and real-time ultrasonography in this field are needed in order to determine the real clinical usefulness of this technique in the study of adrenal gland disease.

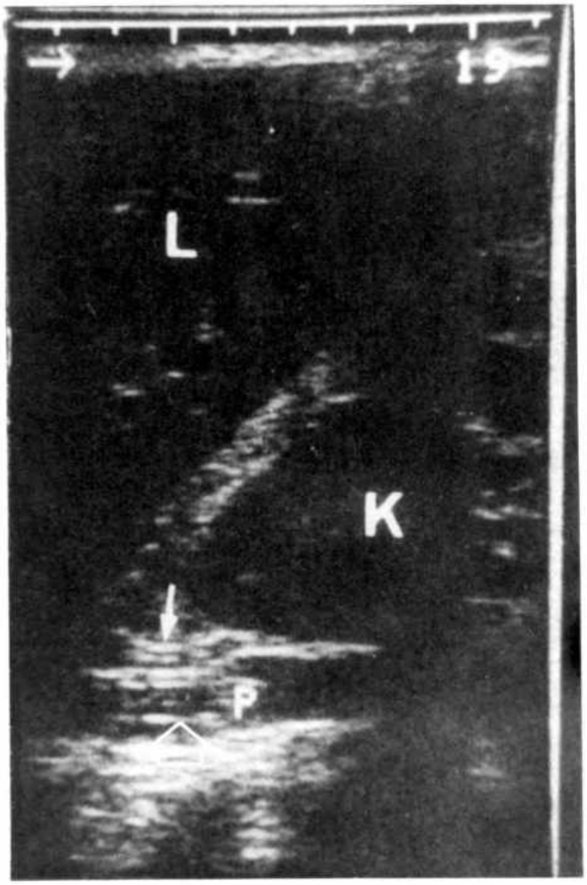
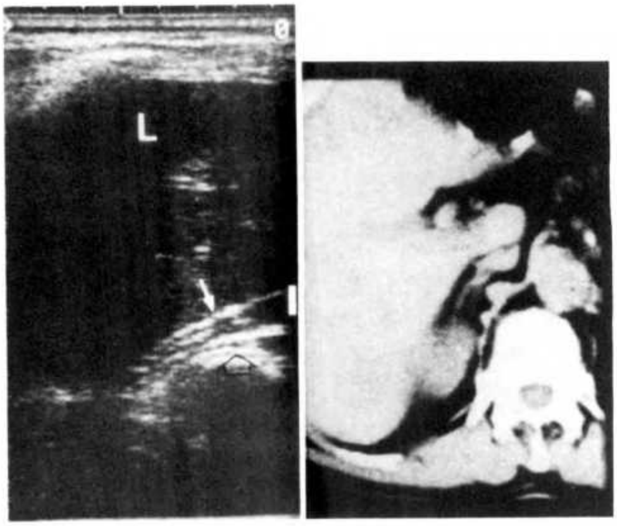


FIG. 7.

Longitudinal scan of the right adrenal. A thin, hyperechogenic line may be seen in the centre of the hypoechogenic structure of the gland, suggesting a three-layered echo pattern. L = liver; K = right kidney; the open arrow indicates the right diaphragmatic crus.



A

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FIG. 8.

(A) Transverse scan of the right adrenal gland. In this subject the gland (arrow) has an asymmetric X shape. The short limbs of the X are directed antero-medially and reach the postero-lateral wall of the inferior vena cava. One of these structures may possibly be interpreted as the central vein of the right adrenal gland. (B) A CT scan of another subject in which the same findings are presented. L = liver; I = inferior vena cava; the open arrow points to the right diaphragmatic crus.

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REFERENCES

ABRAMS, H. L., SIEGELMAN, S. S., ADAMS, D. F., SANDERS, R., FINBERG, H. J., HESSEL, S. J. & MCNEIL, B. J., 1982. Computed tomography versus ultrasound of the adrenal gland: a prospective study. *Radiology*, *143*, 121–128.

BARTRUM, R. J. & CROW, H. C., 1979. Real-time ultrasound: its role in abdominal examination. *Radiology*, *133*, 823–824.

COOPERBERG, P. L., 1983. Sonography without static scanning: sure! *American Journal of Roentgenology*, *141*, 429.

GÜNTER, R. W., KELBEL, C. & LENNER, V., 1984. Real-time ultrasound of normal adrenal glands and small tumors. *Journal of Clinical Ultrasound*, *12*, 211–217.

HUNTER, T. B. & HABER, K., 1983. A comparison of real-time scanning with conventional static B-mode scanning. *Journal of Ultrasound in Medicine*, *2*, 363–368.

LEE, J.K.T., BARON, R. L., MELSON, G. L., MCCLENNAN, B. L. & WEYMAN, P. J., 1981. Can real-time ultrasound replace static B-mode scanning in the diagnosis of renal obstruction? *Radiology*, *139*, 161–165.

MITTY, H. A. & YEH, H.-C., 1982. Anatomy. In *Radiology of the Adrenals with Sonography and CT*. Ed. by H. A. Mitty & H.-C. Yeh (W. B. Saunders, Philadelphia), pp. 1–16.

OPPENHEIMER, D. A., CARROL, B. A. & YOUSEM, S., 1983. Sonography of the normal neonatal adrenal gland. *Radiology*, *146*, 157–160.

SAMPLE, W. F., 1977. A new technique for evaluation of the adrenal gland with gray scale ultrasonography. *Radiology*, *124*, 463–469.

——1978. Adrenal ultrasonography. *Radiology*, *127*, 461–466.

SAMPLE, W. F. & SARTI, D. A., 1978. Computed tomography and gray scale ultrasonography of the adrenal gland: a comparative study. *Radiology*, *128*, 377–383.

SANDERS, R. C., 1979. Real-time ultrasound in abdominal examinations. *Radiology*, *133*, 823–824.

YEH, H.-C., 1980. Sonography of the adrenal glands: normal glands and small masses. *American Journal of Roentgenology*, *135*, 1167–1177.

YEH, H.-C., MITTY, H. A., ROSE, J., WOLF, B. S. & GABRILOVE, J. L., 1978a. Ultrasonography of adrenal masses: usual features. *Radiology*, *127*, 467–474.

YEH, H.-C., MITTY, H. A., ROSE, J., WOLF, B. S., & GABRILOVE, J. L., 1978b. Ultrasonography of adrenal masses: unusual manifestations. *Radiology*, *127*, 475–483.

1986, *The British Journal of Radiology*, 59, 765–771 AUGUST 1986

Imaging of questionable and unusual pelvic masses

By *Karen L. Reuter, M.D., Carl J. D'Orsi, M.D., Vassilios Raptopoulos, M.D. and Kathryn Evers, M.D.

Department of Radiology, University of Massachusetts Medical Center, 55 Lake Avenue North, Worcester, Massachusetts 01605, USA

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ABSTRACT

Ultrasonography is usually the initial diagnostic examination performed for evaluating gynaecological conditions and pelvic masses. The authors' experience with 11 "problem cases" and a review of the literature of such enigmas has led to the following recommendations in the following order: a plain radiograph or repeat ultrasound study; ultrasound study with the water enema technique; gastrointestinal examination if the answer is still not apparent, followed by computed tomography or a real-time ultrasound study during a clinical pelvic examination.

Ultrasonography is usually the initial diagnostic examination performed in the elucidation of gynaecological conditions and pelvic masses because of its superb delineation of the pelvic organs through a fluid-filled bladder. However, difficulties may arise in identifying the origin or underlying pathology of a pelvic mass. This review describes and assesses our experience with questionable and unusual pelvic masses seen by ultrasonography, as well as the experience of others as reported in the literature.

COMMON PROBLEMS

Degree of bladder distension

In order for the pelvic organs to be visualised on ultrasonography, optimal filling of the bladder is to about 2 cm above the uterine fundus. This not only displaces loops of bowel out of the pelvis, but also helps to avoid sound-beam distortion from the pelvic organs. For example, when the bladder is only partially full, the uterine fundus may appear relatively hypoechoic, simulating a leiomyoma. This phenomenon is due to the anterior location of the fundus and the need for overangulation of the transducer, which can result in a suboptimal relationship between the ultrasonic beam and the uterine fundus. However, more often, when the bladder is only partially filled, there is difficulty setting the TGC and overall gain due to an irregular fluid path. Even when imaging through a full bladder, distortion of the sound beam can occur, leading to misdiagnosis. For example, in a patient with a retroverted uterus, the posterior angulation of the uterus is not optimal for the production of echoes, resulting in a hypoechoic image of the fundus that simulates a leiomyoma. On the other hand, overdistension of the bladder distorts the relationship between the uterus and vagina, making it difficult to identify the infantile uterus in a child or post-menopausal woman (Deutsch & Gosink, 1982).

Abnormal pelvic mass versus normal bowel

Distinguishing an abnormal pelvic mass from normal bowel on sonograms may be difficult. Real-time scanning is often helpful in demonstrating areas where peristalsis can be identified (Fleischer et al, 1978, 1982a, b). For example, when a fluid-filled segment of rectosigmoid colon or small bowel is located between the uterus and ovary, mimicking a cystic adnexal mass, real-time ultrasound may reveal peristalsis and resolve the dilemma. Although peristalsis in the small bowel is common, it is rare in the rectosigmoid colon.

Although the sonographic appearance of the rectum can vary widely, the rectosigmoid usually contains gas, which causes high-level echoes and acoustic shadowing (Deutsch & Gosink, 1982). Dermoid tumours, with their complex tissue structure, may be interpreted as normal bowel (Fig. 1A) (Walsh et al, 1979). Physical examination and a plain radiograph interpreted with the sonogram (Fig. 1B) can often resolve the issue.

Confusion can also occur when faecal material filling the large bowel (Fig. 2A) or a large solid tumour of the gastrointestinal tract appears as a solid or mixed pelvic mass on sonographic images (Fleischer et al, 1978). Kurtz et al (1979) suggest a repeat ultrasound study following a cleansing enema to differentiate bowel from a pelvic mass. A Dulcolax suppository (Windsor Pharmaceuticals) can also be used (Fig. 2B). In two of our cases, evacuation and cleansing enemas did not alter the appearance of the "mass".

Water enema technique

To distinguish faeces from abnormal findings, some authors (Fleischer et al, 1978; Rubin et al, 1978; Fleischer et al, 1982b, c, Lewis et al, 1982) recommend a water or isotonic saline enema with filling of the rectum and rectosigmoid, and a distended bladder (Fig. 3). The major pelvic organs are usually not completely defined in pre-water sonograms. Likewise, the caudal extent of the intraperitoneal space (pouch of Douglas) is not usually seen in pre-water sonograms unless fluid, such as ascites, is present (Yeh & Wolf,

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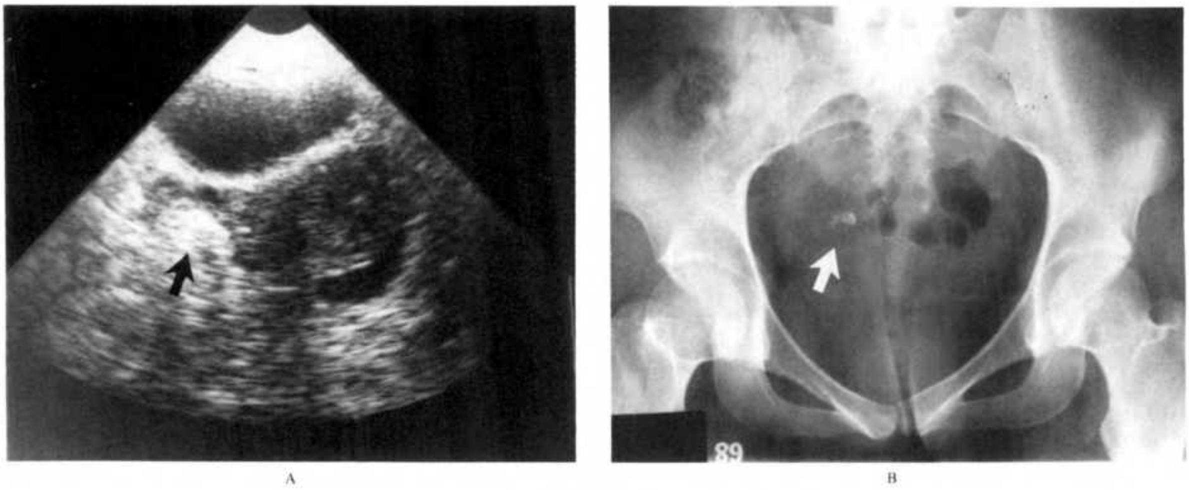

FIG. 1.

Dermoid tumour. (A) Transverse real-time sonogram showing increased echoes of the right adnexa (arrow) without the appearance of a defined mass. Note free fluid in the pouch of Douglas. (B) Radiograph showing a lucent pelvic mass with a "tooth" in the right side of the pelvic inlet (arrow).

1977). With the water enema technique one can locate the large bowel, particularly the rectum, sigmoid, caecum, and interfaces between the bowel and the pelvic organs (Fleischer et al, 1982b). When filled with fluid, the rectum often becomes a sonic window to the sacrum, demarcating the relationship between these two structures. Rubin et al (1978) have found that when the water enema fails to distend the colon, insufflation of air during real-time sonography will often reveal the location of the colon.

We have found the water enema technique to be very helpful. In one patient, pre-water sonography was followed by sonography with a tap-water enema to delineate the retained cervix better and to exclude recurrent tumour after chemotherapy (Fig. 3A). The ultrasound images correlated with the surgical findings,

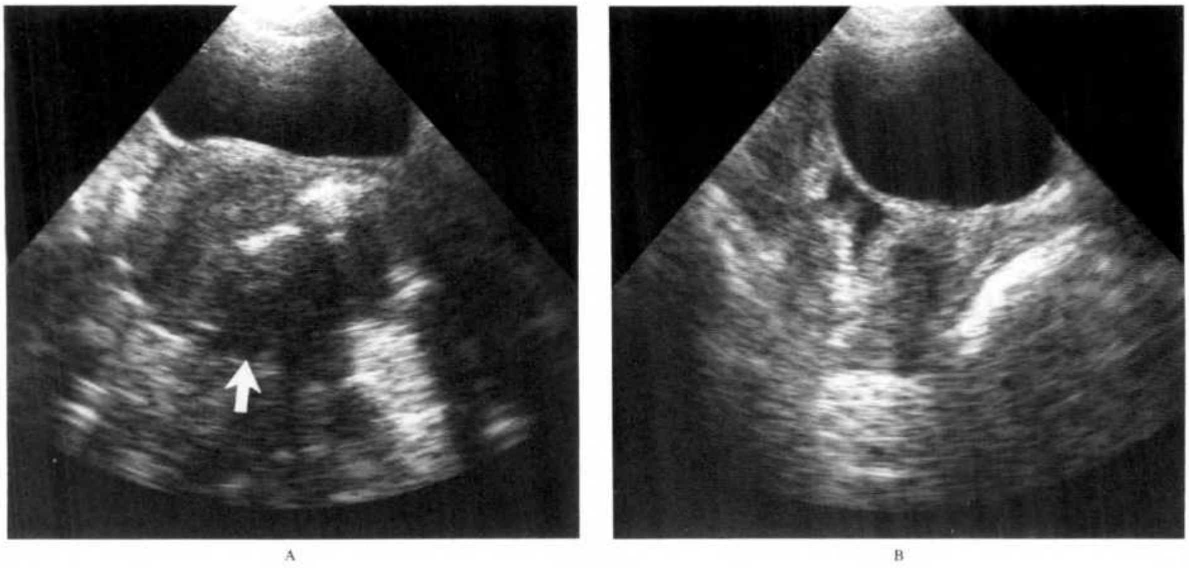

FIG. 2.

Retroverted uterus and rectosigmoid pseudotumour before and after evacuation. (A) Sagittal sonogram showing increased echoes with acoustic shadowing posterior to the uterus (arrow). (B) Sagittal ultrasound after a Dulcolax suppository; the previous abnormalities are no longer present.

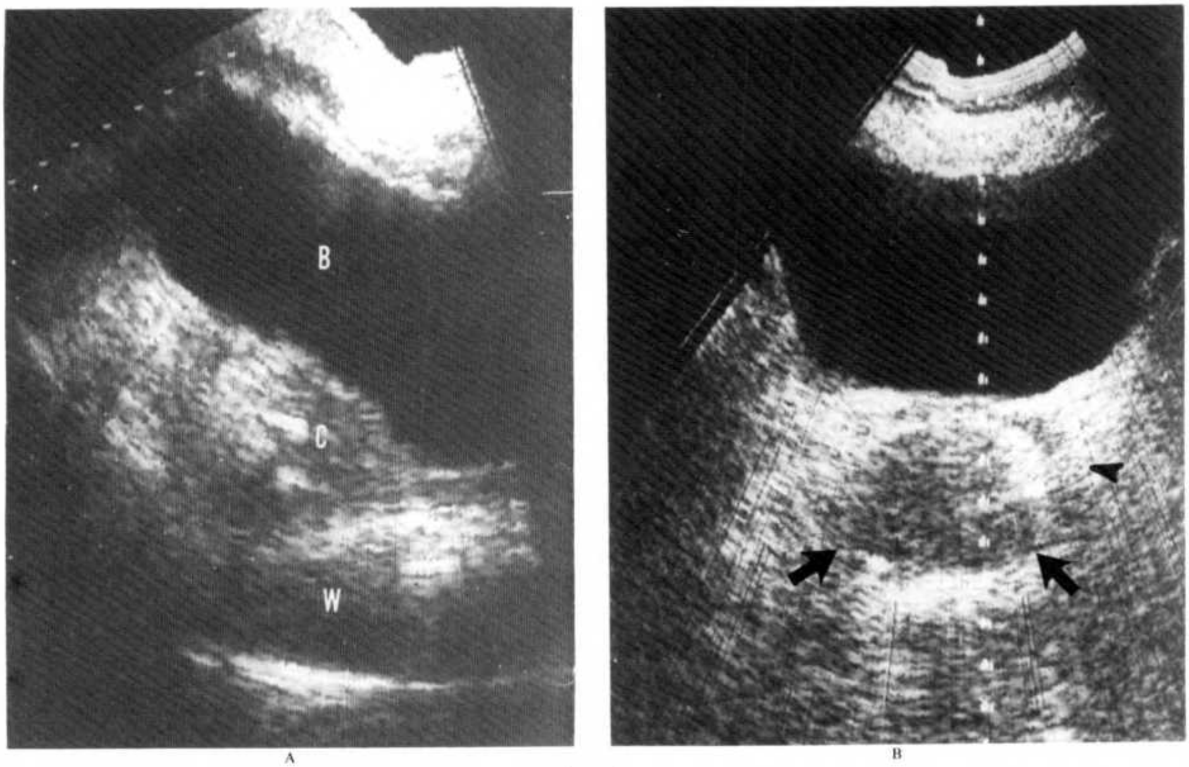

FIG. 3.

Delineation of a true pelvic mass with the water enema technique. (A) Sagittal ultrasound scan of the retained cervix following the water enema (B = bladder, C = retained cervix, W = water). (B) Transverse sonogram at the level of the symphysis pubis after 200 ml of tap water was instilled per rectum shows no change in the mass (arrows); swirling echoes from the water (arrowhead) were seen to the left of the mass with real-time sonography.

showing the pelvis to be free of tumour, with some fibrosis of the retained cervix. In another patient, the ultrasound study with the water technique showed water flowing to the left of a persistent right-sided pelvic mass (Fig. 3B). Sequential computed tomography (CT) scans performed to evaluate the liver for biopsy confirmed the pelvic mass. Sigmoidoscopy showed extrinsic pressure upon the sigmoid colon and exploratory laparotomy subsequently disclosed a 5 cm spherical pelvic mass of recurrent endometrial carcinoma.

Uterine versus adnexal mass

Ultrasound studies are frequently requested to determine whether a palpated pelvic mass in a female is of uterine or adnexal origin. Uterine smooth muscle tumours have no pathognomonic ultrasound appearance, but the more common leiomyomas (intramural leiomyomas) distort the uterine outline and create an enlarged uterus, often irregular in contour. Subserosal leiomyomas protrude beyond the uterine outline and, thus, may simulate solid ovarian lesions (Walsh, 1979; Walsh et al, 1980). In one of our cases, the history and physical examination of the patient suggested uterine myomas, but the ultrasound image showed three hypoechoic masses suggestive of ovarian masses abutting the uterus (Fig. 4). In contrast to this case of echo-poor parametrial leiomyomas, Nocera et al (1984) recently reported two cases of cystic parametrial fibroids mimicking ovarian cystadenomas. Furthermore, extensive cystic degeneration of a leiomyoma has been misdiagnosed on sonograms as a molar pregnancy or ovarian cyst (Gottesfeld, 1979; Walsh, 1979). We interpreted a case of a ruptured ectopic pregnancy presenting with gastrointestinal distress and a positive human chorionic gonadotrophin test as a molar pregnancy because of the large amount of adherent blood, which made the uterus appear enlarged (Fig. 5). At surgery, the initial impression was that of a large, haemorrhagic uterine neoplasm before the correct diagnosis became evident.

Ultrasound versus computed tomography

Ultrasound has been the primary modality for assessing pelvic malignancies, but the role of CT in the pelvis has increased. Although the most operator-dependent modality (Lewis et al, 1982), ultrasound is the most revealing modality for the detection of ovarian

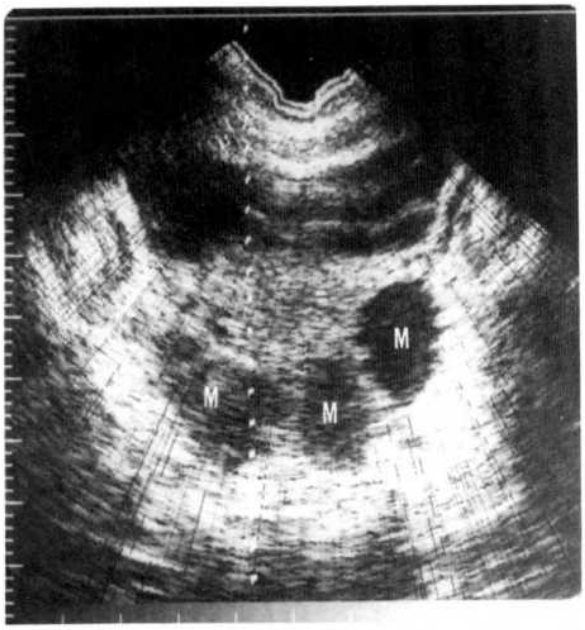

Fig. 4.

Uterine leiomyomas mimicking adnexal masses. Transverse sonogram 3.2 cm above the symphysis pubis shows three masses abutting the uterus (M = mass).

masses, being more consistent than CT in determining the ovarian origin of pelvic masses (Walsh, 1979). Also, CT does not depict normal ovaries as clearly as does ultrasound (Walsh et al, 1978). Walsh reported that cervical carcinoma is more clearly demonstrated by ultrasound studies than by CT, since both sagittal and transverse scans can be obtained with ultrasound (Walsh, 1979) while, with real-time scanning, any plane giving a good image is feasible. However, reconstruction of CT images in sagittal, coronal, paraxial and oblique modes also allows CT multiplanar imaging. A technically adequate sonographic study may reveal a mass smaller than 2 cm in diameter because of its echo-free nature and sharply defined margin, but a solid mass less than 2 cm in size may escape recognition (Lewis et al, 1982). Computed tomographic imaging with contrast-filled bowel and scans at 1 cm intervals would be more likely to detect a small, solid mass.

Neither modality is without shortcomings, but it is becoming clearer which one is better in specific instances. Sanders et al (1983), investigating recurrences of carcinoma of the cervix, endometrium and ovary in 110 patients, recorded five examples of peritoneal studding missed by CT and one missed by ultrasound, four vaginal lesions not seen with ultrasound and three not seen with CT and bladder involvement not seen with CT. Recurrent tumours were detected with equal accuracy by both ultrasound and CT. Both modalities

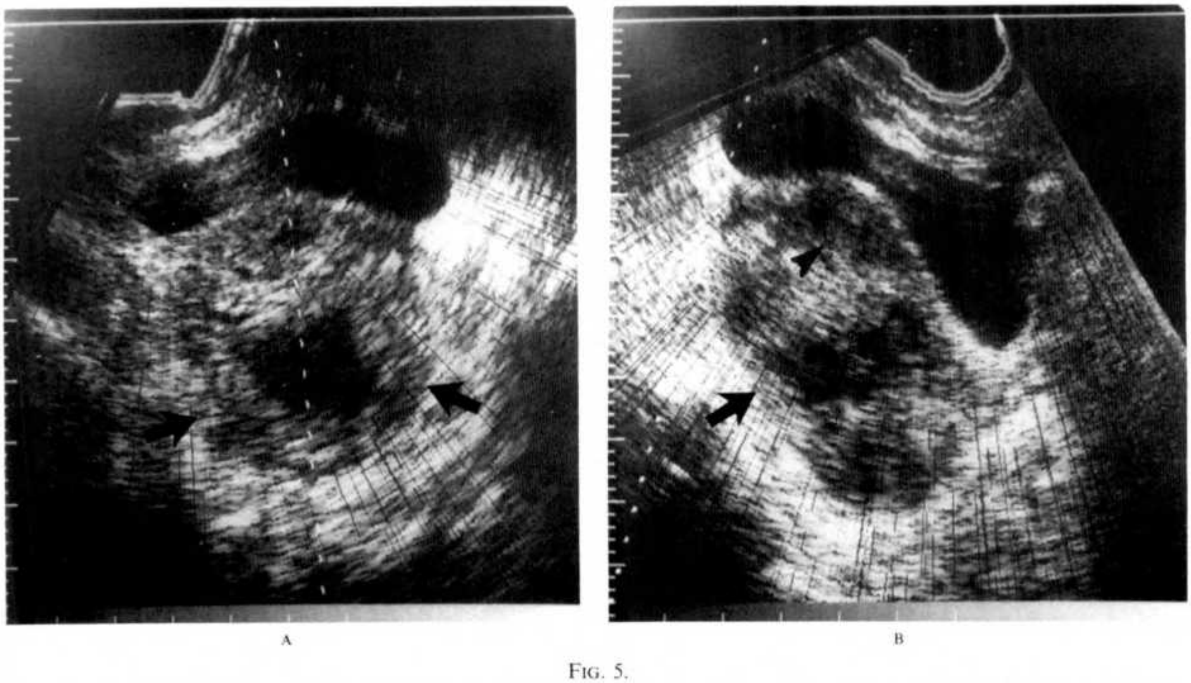

Fig. 5.

Ectopic pregnancy mimicking a molar pregnancy. (A) Transverse sonogram 4.1 cm above the symphysis pubis shows apparent enlargement of the uterus (arrows). (B) Sagittal ultrasound image 0.7 cm to the right of the midline shows the apparent uterine enlargement to be due to adherent blood (arrow). Arrowhead points to the actual posterior uterine wall. Distance between dots = 1 cm.

were less accurate in the detection of associated lesions away from the original tumour site. Walsh et al (1980) reported that lateral pelvic wall nodes from cervical carcinoma as small as 2 cm have been imaged by sonography. However, CT was more sensitive than ultrasound for identifying pelvic adenopathy or para-aortic adenopathy in a study by Walsh (1979). In endometrial carcinoma, Brascho et al (1978) concluded

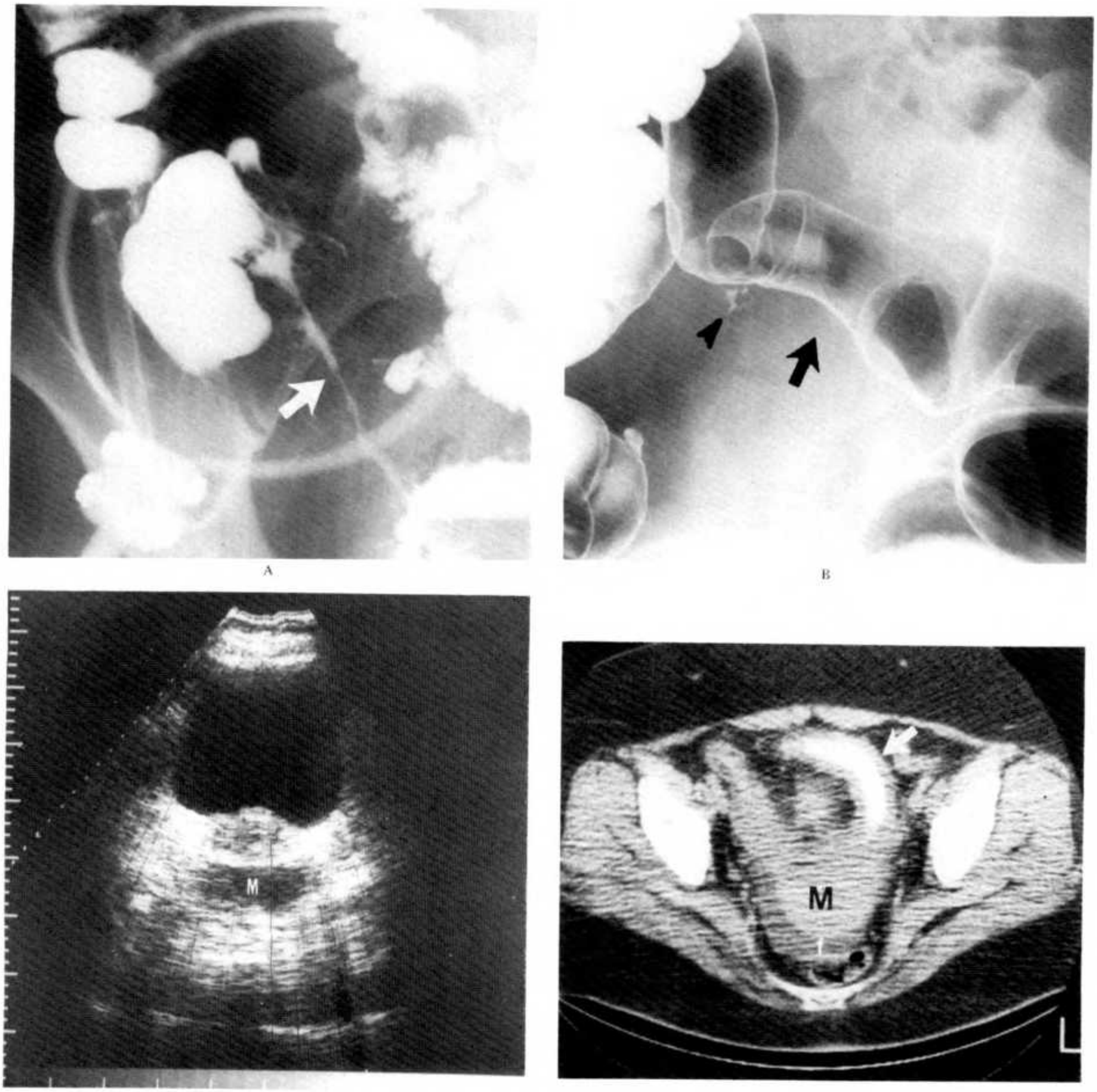
A B C D

FIG. 6.

Crohn's disease of the small bowel presenting as a pelvic mass. (A) Small-bowel barium enema demonstrates 18 cm of narrowed, fixed terminal ileum (arrow), devoid of the normal valvulae conniventes. (B) Lateral spot film of rectosigmoid colon from the double-contrast barium enema showing compression by an extrinsic mass (arrow). Note extravasation of contrast material from the sigmoid colon (arrowhead). (C) Transverse sonogram about 0.5 cm above the symphysis shows a hypoechoic, ill-defined mass in the pouch of Douglas (M) (5 cm transversely × 3 cm deep × 6 cm long) with poor posterior wall acoustic enhancement. (D) A CT scan at the level of the fifth sacral vertebra reveals fluid in the pouch of Douglas (f), an ill-defined retrouterine solid mass (M), and 8 cm thickening (arrow) of the wall of a small-bowel loop.

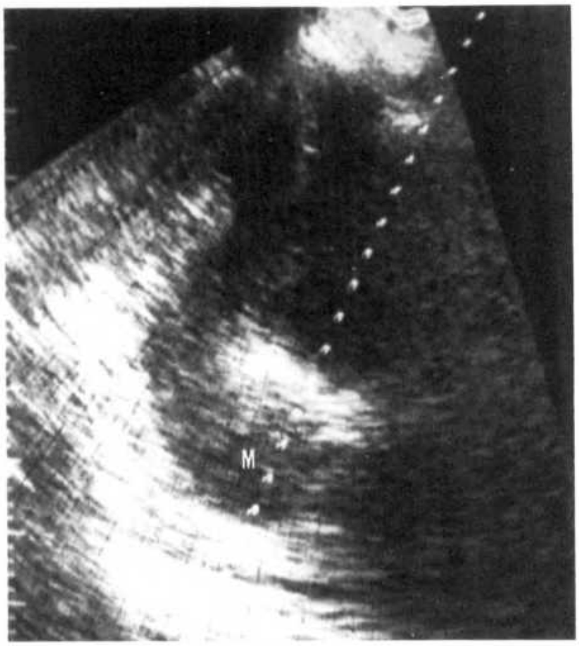

Fig. 7.

Mesentery mimicking a pelvic mass. Sagittal sonogram showing an echogenic mass (M) posterior to the bladder.

that ultrasound does not give optimal results in the detection of tumour extension beyond the serosal surface unless the lesion is massive. For staging pelvic malignancies, CT scanning is the modality of choice because it clearly shows pelvic wall extension and any bony involvement. Abdominal organ involvement with tumour, lymphadenopathy, and pulmonary metastases are also well imaged by CT, and density measurement of lesions is an additional advantage. For detecting or determining the presence of the organ of origin of a pelvic mass, ultrasound appears to be the modality of choice.

Choice of studies for characterising a pelvic mass

The question arises as to which diagnostic modality is the most helpful for further assessing a mass seen on ultrasound. The only additional study needed may be a follow-up ultrasound scan, performed after a cleansing enema or suppository to induce evacuation (Fig. 2), or after normal evacuation or a pelvic radiograph (Fig. 1B). But if a "mass" persists on serial sonograms, even after evacuation, the water enema technique may be necessary to differentiate the bowel lumen from the surrounding pelvic organs (Fig. 3).

Barium examination will often be definitive (Bell & Burke, 1982). In three of our 11 patients, gastrointestinal examination provided the necessary information. In one patient, the absence of a mass in the region of the rectosigmoid was shown by proctosigmoidoscopy, colonoscopy and a barium enema study; in a second, normal bowel was diagnosed by a barium enema alone. In the third patient, the diagnosis was determined by large- and small-bowel barium examinations (Fig. 6A, B), which clearly showed a deformed caecum and a fixed terminal ileum. Sequential sonography performed to delineate the pelvic mass revealed an unchanging mass about 0.5 cm above the symphysis pubis (Fig. 6C). A subsequent CT scan showed a soft-tissue mass and a thick-walled loop of small bowel (Fig. 6D). Surgery confirmed the diagnosis of Crohn's disease and also revealed matted small-bowel loops in the pelvis and both ileocolonic and ileovesical fistulae.

Consultation with the surgeon regarding a post-operative sonogram can also provide important information as to the nature of an apparent pelvic mass. The echogenic "mass" seen in Fig. 7 remained unchanged sonographically over 1 week and was proved at autopsy to be fatty mesentery placed behind the bladder at the time of bowel resection for a colorectal fistula.

Physical examination of the pelvis during real-time sonographic scanning has recently been discussed in one publication (Bluth et al, 1984). This co-operative endeavour may make other modalities unnecessary and can sometimes resolve the diagnostic dilemma. The value of this technique was evident in one of our cases in whom echoes were seen as the examining finger ballotted the suspected "pelvic mass". The relationship of the "mass" to the pelvic organs then became apparent. The questionable mass felt like normal bowel to the examiner and could be seen to lie around the examining finger in the rectum during real-time scanning; this finding was verified by a barium enema.

For pelvic pathology, CT can be complementary to ultrasound in complicated cases and can serve as the primary modality for the staging of malignancy or for evaluating disease that extends to the pelvic walls. Computed tomography is relatively expensive, however, and its use as a screening or primary modality may not be cost effective (Walsh et al, 1978).

CONCLUSION

From our own experience and a review of the literature, we recommend that for characterising a pelvic mass seen by ultrasonography, a plain radiographic study or repeat ultrasound examination be performed and correlated with the history and physical examination. An ultrasound study combined with the water enema technique is suggested as the next examination, followed, if necessary, by a barium examination of the gastrointestinal tract, a CT scan or a real-time ultrasound study during a clinical pelvic examination. In most cases, close correlation with the history and physical examination may lead to the proper sonographic interpretation. Sometimes, however, the correct imaging interpretation becomes apparent only after surgery.

REFERENCES

BELL, M. R. & BURKE, A., 1982. Fictitious masses with pelvic imaging. *Medical Journal of Australia, 2,* 173–174.

BLUTH, E I, FERRARI, B. T & SULLIVAN, M. A., 1984 Real-time pelvic ultrasonography as an adjunct to digital examination. *Radiology, 153,* 789–790.

BRASCHO, D. J, KIM, R. Y. & WILSON, E. E., 1978. Use of ultrasonography in planning intracavitary radiotherapy of endometrial carcinoma *Radiology, 129,* 163–167.

DEUTSCH, A L & GOSINK, B. B., 1982. Normal female pelvic anatomy. *Seminars in Roentgenology, 17,* 241–250

FLEISCHER, A. C., BOEHM, F. H. & JAMES, A. E., JR, 1982a. Sonography and radiology of pelvic masses and other maternal disorders. *Seminars in Roentgenology, 17,* 172–181.

FLEISCHER, A. C., JAMES, A. E., JR, MILLIS, J. B. & JULIAN, C., 1978 Differential diagnosis of pelvic masses by gray scale sonography. *American Journal of Roentgenology, 131,* 469–476.

FLEISCHER, A. C., MUHLETALER, C. A., KURTZ, A. B. & JAMES, A. E., JR, 1982b. Real-time sonography of bowel. *Clinics in Diagnostic Ultrasound, 10,* 117–135.

FLEISCHER, A. C., WALSH, J. W., JONES, H. W., III, CHUANG, V. P. & WALLACE, S., 1982c. Sonographic evaluation of pelvic masses: method of examination and role of sonography relative to other imaging modalities. *Radiologic Clinics of North America, 20,* 397–412.

GOTTESFELD, K. R., 1979 The role of ultrasound in gynecologic diagnosis. In *Genitourinary Ultrasonography.* Ed. by A. T. Rosenfield (Churchill Livingstone, New York), pp. 207–227.

KURTZ, A. B., RUBIN, C. S., KRAMER, F. L. & GOLDBERG, B B, 1979. Ultrasound evaluation of the posterior pelvic compartment. *Radiology, 132,* 667–682.

LEWIS, E., ZORNOZA, J., JING, B. S., SCHAFF, M. I. & JAMES, A E., JR, 1982. Radiologic contributions to the diagnosis and management of gynecologic neoplasms. *Seminars in Roentgenology, 17,* 251–268.

NOCERA, R. M, FAGAN, C. J. & HERNANDEZ, J C., 1984. Cystic parametrial fibroids mimicking ovarian cystadenoma. *Journal of Ultrasound in Medicine, 3,* 183–187.

RUBIN, C. S., KURTZ, A B. & GOLDBERG, B. B., 1978. Water enema: a new ultrasound technique in defining pelvic anatomy. *Journal of Clinical Ultrasound, 6,* 28–33.

SANDERS, R. C., MCNEIL, B. J., FINBERG, H. J., HESSEL, S. J., SIEGELMAN, S. S., ADAMS, D. F., ALDERSON, P O. & ABRAMS, H L., 1983. A prospective study of computed tomography and ultrasound in the detection and staging of pelvic masses. *Radiology, 146,* 439–442.

WALSH, J. W., 1979 Comparison of ultrasound and computed tomography in the evaluation of pelvic masses. *Clinics in Diagnostic Ultrasound, 2,* 229–242.

WALSH, J. W., BREWER, W. H. & SCHNEIDER, V., 1980. Ultrasound diagnosis in diseases of the uterine corpus and cervix *Seminars in Ultrasound, 1,* 30–40.

WALSH, J. W., ROSENFIELD, A. T., JAFFE, C C., SCHWARTZ, P. E., SIMEONE, J., DEMBNER, A. G. & TAYLOR, K. J. W., 1978. Prospective comparison of ultrasound and computed tomography in the evaluation of gynecologic pelvic masses. *American Journal of Roentgenology, 131,* 955–960

WALSH, J. W., TAYLOR, K. J. W., WASSON, J. F M., SCHWARTZ, P E. & ROSENFIELD, A. T., 1979. Gray-scale ultrasound in 204 proved gynecologic masses: accuracy and specific diagnostic criteria. *Radiology, 130,* 391–397.

YEH, H. C & WOLF, B. S., 1977. Ultrasonography in ascites. *Radiology, 124,* 783–790.

Book reviews

Paediatric Diagnostic Imaging. By Catherine Gyll and Noel Blake, pp viii+227+index, 1985 (Heinemann, London), £29 95
ISBN 0-433-12700-7

In the preface to this excellent book the authors state, "The standard of paediatric radiography in general hospitals can be improved only by knowledgeable senior radiographers, and by radiologists who are aware of how the radiographs, on which they report, have been produced". The book aims to increase this knowledge and awareness by descriptions of the radiographic techniques more suited to children, with advice on immobilisation and protection, and notes on paediatric pathology The chapters are well set out, and the numerous illustrations are of a very high standard.

Advice on handling and immobilisation is very sensible and practical, but it is surprising that two helpers holding on either side of the patient is not preferred to one person (however suitably protected) holding in the direct beam The comments on special paediatric screening units would not meet with the approval of all paediatric radiologists.

The chapter on chest and neck radiography is particularly good, and the many reproductions of radiographs show the high standard it is possible to attain using simple methods. Another outstanding chapter is the one on limb injuries. Difficulties experienced in producing accurate projections with the minimum upset to the patient will be largely solved by following the authors' advice.

A wealth of information is contained in the section on the new-born infant from advice on film-screen combinations, descriptions of incubators and life-support systems to handling techniques, reasons for requests and common faults in radiographic technique. Reference is made to the roles of sonography, computed tomography and radionuclide imaging in the care of the neonatal patient.

The last section of the book, rather unfortunately called "Imaging Scans", is not as detailed, and is more controversial than the rest, but achieves its aim of showing the place of the new modalities in the paediatric field.

The book will be invaluable to the training programme in paediatric X-ray departments and as a reference book in general X-ray departments. For radiographers and radiologists wishing to improve the standard of paediatric diagnostic imaging in their departments, it is a very worthwhile purchase.

ELIZABETH MARION NEILL

Cancer of the Female Reproductive System. Ed. by Christopher J. Williams and J Michael A. Whitehouse, pp. 370, 1985 (John Wiley & Sons, Chichester), £39.50.
ISBN 0-471-90470-8

This is the third volume of a series of books concerned with cancer assessment and management. The editors have assembled 36 authors to contribute 26 chapters on different aspects of both problems. The contributors are well chosen for their acknowledged experience and interest in gynaecological oncology and they have produced a series of essays. In fairness to the individuals, the majority of these are well written, clear and concise. The different primary tumours are dealt with satisfactorily within this framework, but in the investigational chapters there is a strong impression of dragging out the relevance of the different aspects of the imaging techniques. Sequential reading of the chapters in this region does not lead to the construction of a logical investigational scheme. Enthusiasts can present a well constructed and appealing case for, for example, clonogenic assays, histological grading or for hormone receptor measurement. I felt a need for a balanced overview of these different aspects of investigation. The literature is replete with review articles on the different subjects. To be valuable to busy clinicians or trainees this book needed to be edited to draw the experience of the different authors together. Otherwise it is the state of the art 1985, and it is now 1986

R D. HUNTER

1986, *The British Journal of Radiology*, 59, 773–777 AUGUST 1986

False positive localisation of indium-111 granulocytes in colonic carcinoma

By Sethna H. Saverymuttu, M.R.C.P., Paul Maltby, Phillip Batman, M.B., B.S., Anton E. Joseph, F.R.C.R. and Douglas Maxwell, F.R.C.P.

Departments of Medicine, Pharmacy, Pathology and Nuclear Medicine, St George's Hospital, Blackshaw Road, London SW17

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ABSTRACT

Indium-111 leucocyte scanning has been shown to be a highly accurate technique for detecting abscesses and assessing inflammatory bowel disease. We have encountered two cases of colonic carcinoma which presented as suspected inflammatory bowel disease and were found to localise ^{111}In-labelled granulocytes. Histology revealed an acute inflammatory infiltrate in these tumours. These results indicate that ^{111}In granulocyte scanning has limitations in the diagnosis of inflammatory bowel disease.

Indium-111 labelled leucocyte scanning has been established as an accurate imaging technique in the diagnosis of abscesses (Segal et al, 1976; Knochel et al, 1980; Carroll et al, 1981; Saverymuttu et al, 1983a). It has the advantage over gallium of providing a rapid result and avoiding problems with false positive localisation due to tumours, renal tract or bowel excretion. This lack of bowel excretion has led to its widespread use in the assessment of disease distribution and activity in inflammatory bowel disease (IBD) (Segal et al, 1980; Saverymuttu et al, 1982, 1983b; Stein et al, 1983). Indeed, it has been suggested that "this procedure may become the routine mechanism for identifying recurring inflammatory colitis" (Froelich & Swanson, 1984) and has the potential in IBD for diagnosis, staging and monitoring response to treatment (Kipper & Williams, 1982).

A high degree of specificity has been reported with ^{111}In leucocyte scanning, ranging from 90–100%, both for abdominal abscesses (Segal et al, 1976; Knochel et al, 1980; Carroll et al, 1981; Saverymuttu et al, 1983a) and also for IBD (Froelich & Swanson, 1984; Saverymuttu et al, 1983c). However, recent studies have noted some non-specificity with ^{111}In activity in rejecting renal transplants (Frick et al, 1979) and haematomas (Wing et al, 1984). These false positives might be explained by contaminating platelets or mononuclear cells, which, according to recent estimates, comprise a large proportion of ^{111}In activity on the standard mixed leucocyte preparation (Dewanjee, 1984; Dewanjee et al, 1984). The mixed leucocyte preparation has recently been modified to increase its specificity for acute inflammation by labelling a pure granulocyte fraction free from platelet and mononuclear cell contamination (Danpure et al, 1982; Saverymuttu et al, 1983b). Despite the need for an additional separation stage, viability has been preserved by maintaining granulocytes in plasma during separation and labelling in plasma with ^{111}In tropolonate. These cells demonstrate rapid localisation in sites of inflammation (Peters et al, 1983; Saverymuttu et al, 1983d).

We have recently noted false positive localisation of ^{111}In granulocytes in two cases of suspected inflammatory bowel disease who subsequently were shown at laparotomy to have colonic carcinoma.

CASE REPORTS

Case 1

A 65-year-old woman presented with intermittent colicky abdominal pain with watery diarrhoea for the previous 6 months. Examination was normal, as were routine laboratory studies apart from an erythrocyte sedimentation rate (ESR) which was raised at 44 mm in the first hour. Radiology was suggestive of caecal narrowing thought to be due to an infiltrating carcinoma or Crohn's disease (Fig. 1). An ^{111}In granulocyte scan (Saverymuttu et al, 1983b), performed with views at 1 h and 3 h, showed mild caecal inflammation (Fig. 2). Laparotomy showed a caecal tumour without evidence of local perforation or abscess formation. Histology showed a Duke's B carcinoma with a mild acute inflammatory infiltrate.

Case 2

A 60-year-old woman presented with a 3-month history of subacute intestinal obstruction with intermittent diarrhoea, associated with 14 lb weight loss. There was no history of rectal bleeding. She was anaemic (Hb 10.7 g/dl), hypoalbuminaemic (albumin 30 g/l), but the ESR was normal. Small-bowel enema, the initial investigation, showed delayed small-bowel transit and some dilated loops but no definite site of obstruction. An ^{111}In granulocyte scan showed intense localisation in the region of the hepatic flexure on the 1 h and 3 h scans (Fig. 3). Barium enema revealed a carcinoma at the hepatic flexure which was resected at laparotomy (Fig. 4). Again, there was no evidence of perforation or local abscess formation to account for the positive scan. Histology showed Duke's B carcinoma with a prominent acute inflammatory infiltrate (Figs 5 and 6).

Address for correspondence: Dr S. H. Saverymuttu, Department of Medicine, St George's Hospital Medical School, Cranmer Terrace, London SW17.

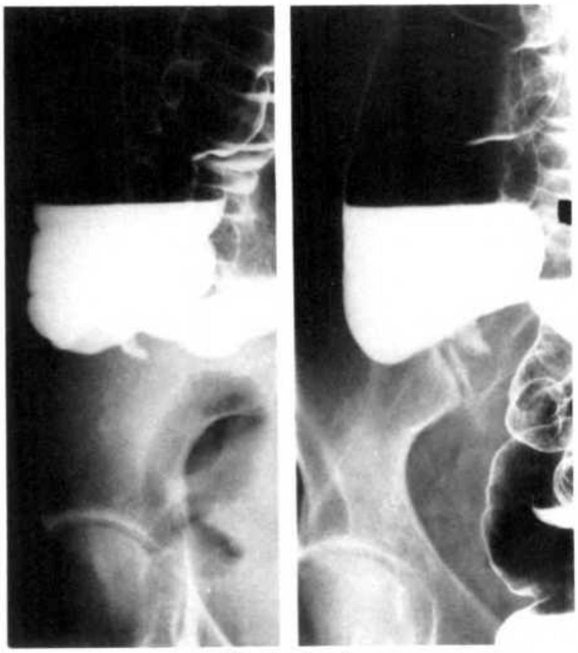

FIG. 1. *Case 1.*
Barium enema showing an abnormal lower pole of the caecum due to a caecal carcinoma.

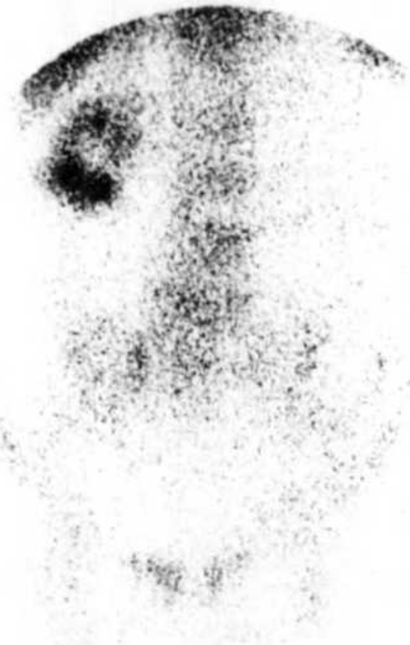

FIG. 3. *Case 2.*
Abdominal scan 1 h after injection of labelled granulocyte showing in addition to the normal distribution of activity in the liver, spleen and bone marrow there is intense abnormal activity in the right upper quadrant corresponding to the hepatic flexure carcinoma.

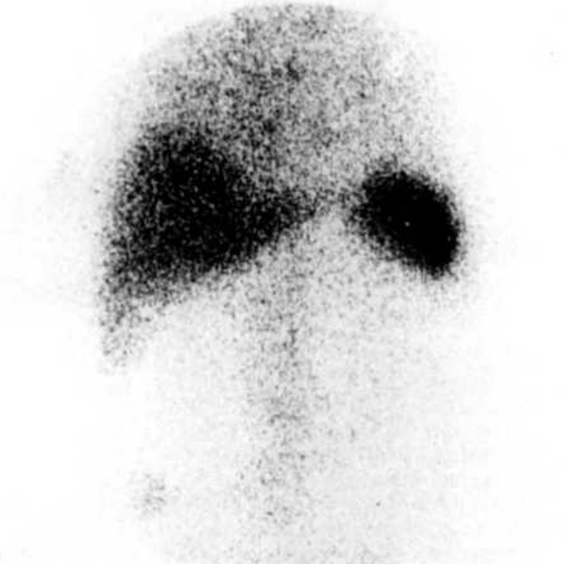

FIG. 2. *Case 1.*
Abdominal scan 1 h after injection of labelling granulocyte showing, in addition to the normal activity in liver, spleen and bone marrow of the lumbar spine, that there is focal activity in the right iliac fossa corresponding to the caecal carcinoma.

DISCUSSION

There is a need to improve our diagnostic approach to IBD. Recent studies have shown the standard approach based on clinical assessment, barium studies and laboratory tests is inadequate, a definite diagnosis of Crohn's disease being made in only 6–20% of cases after initial investigations (Dyer & Dawson, 1970; Admans et al, 1980). Several factors contribute to difficulties in diagnosis, including the large degree of overlap in symptoms with the ubiquitous irritable bowel syndrome (Thompson, 1984) and suboptimal or equivocal radiology. Furthermore, it is now known that good-quality bowel radiology can miss extensive inflammatory bowel disease (Elliott et al, 1982; Kingham et al, 1982). Indium-111 leucocyte scanning should be the ideal imaging procedure for diagnosing IBD since it is non-invasive, screens both small and large bowel in the single investigation and depends on the presence of inflammation. Furthermore, in small-bowel disease where a barium follow-through is equivocal and the lesions inaccessible to endoscopy, ^{111}In leucocyte scanning might provide an alternative to laparotomy. In an early study using the standard mixed leucocyte preparation, no positive results were

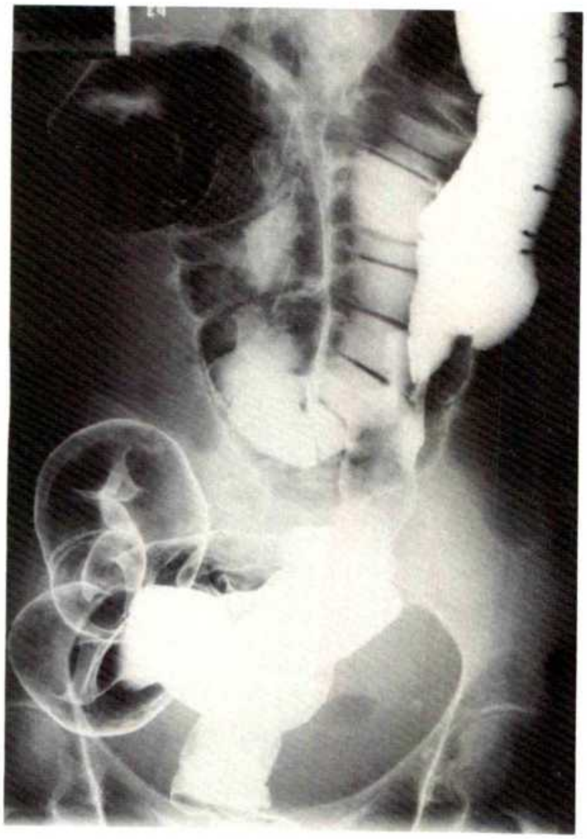

FIG. 4. *Case 2.*
Barium enema showing obstruction at the hepatic flexure due to a carcinoma.

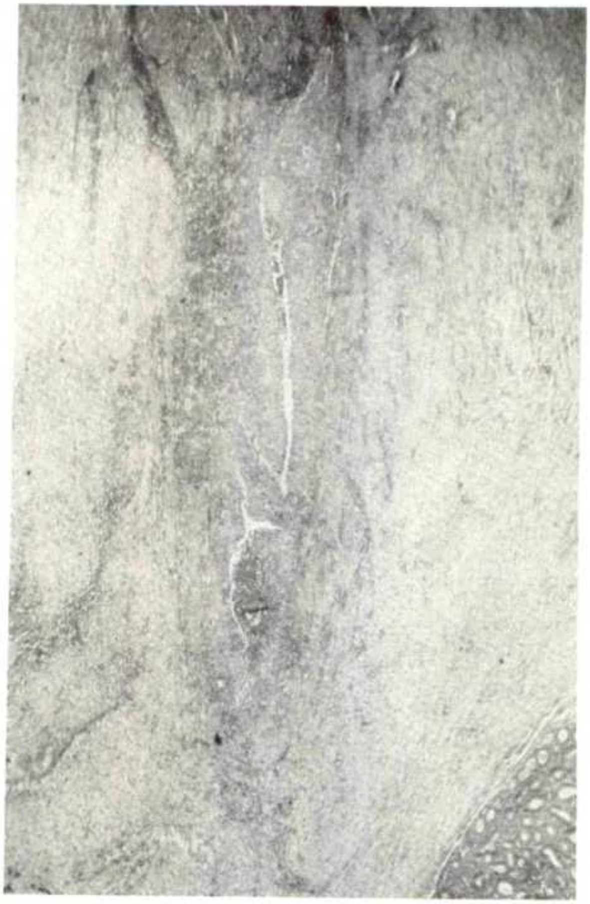

FIG. 5.
Inflammatory infiltrate adjacent to the advancing edge of colonic adenocarcinoma (bottom right). Haematoxylin and eosin (H&E) × 17.

noted in the irritable bowel syndrome and a variety of non-inflammatory bowel diseases including bowel carcinoma (Saverymuttu et al, 1983c). More recently, the more specific preparation, ^{111}In-labelled granulocytes, has been used prospectively to detect IBD and found to be more sensitive than full bowel radiology, without any false positives (Saverymuttu et al, 1985). However, no gut carcinomas were included in this study.

The present report illustrates the limitations of leucocyte scanning in the diagnosis of IBD, but it should be remembered that this limitation does not apply to its value in assessing known cases of IBD. Previous reports demonstrating false positive localisation may be explained by the scanning technique or cell preparation used. For example, positive scans due to swallowed leucocytes (Coleman & Welch, 1980) would have been negative if early scans (within 4 h of injection) had been performed. In the case of rejecting renal transplants (Frick et al, 1979), haematomas (Wing et al, 1984), tumours such as histiocytic lymphomas (McDougall et al, 1979) or skeletal metastases (Sfakianakis et al, 1982), localisation could be due to contaminating platelets or mononuclear cells (Dewanjee et al, 1984; Dewanjee, 1984). It would be expected that ^{111}In granulocyte scans would be negative in these cases. However, the present report highlights the well known histological feature that necrosis with an acute inflammatory infiltrate may occur in many colonic tumours (Kissane, 1985). Under the circumstances, although ^{111}In granulocyte scanning correctly identified inflammation (and so, technically, was a true positive scan), the result was misleading since the test has until now been regarded as specific for inflammatory bowel disease. It is surprising that more false positives due to tumours have not been reported but this may reflect the reduced sensitivity of the standard mixed leucocyte preparations, compared with the pure granulocyte preparation, in localising acute inflammation. Despite these false positive results in colonic tumours, ^{111}In granulocyte scanning remains a valuable technique in

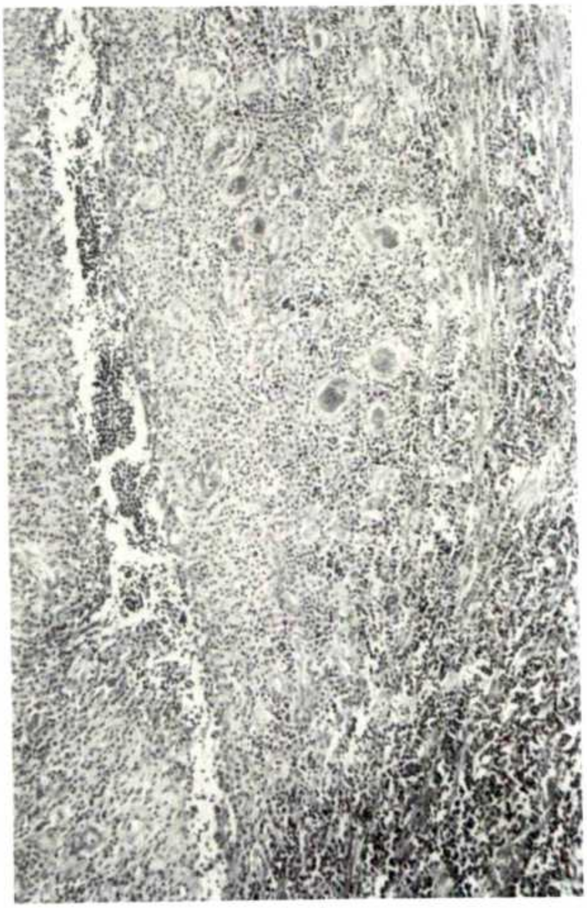

FIG. 6.

High-power view of the inflammatory area showing an infiltrate of polymorph leucocytes and necrotic debris among serosal connective tissue (H&E × 70).

assessing known cases of IBD and has the potential to become the procedure of choice for assessing therapeutic regimes. However, the present cases clearly demonstrate the pitfalls of ^{111}In granulocyte scanning in the diagnosis of IBD and stress the need for independent confirmation.

REFERENCES

ADMANS, H., WHORWELL, P. J. & WRIGHT, R., 1980. Diagnosis of Crohn's disease. *Digestive Diseases and Science*, *25*, 911–915.

CARROLL, B., SILVERMAN, P. M., GOODWIN, D. A. & McDOUGALL, I. R., 1981. Ultrasonography and indium-111 white blood cell scanning for the detection of intra-abdominal abscesses. *Radiology*, *140*, 155–160.

COLEMAN, R. E. & WELCH, D., 1980. Possible pitfalls with clinical imaging of indium-111 leucocytes: concise communication. *Journal of Nuclear Medicine*, *21*, 122–125.

DANPURE, H. J., OSMAN, S. & BRADY, F., 1982. The labelling of blood cells in plasma with ^{111}indium tropolonate. *British Journal of Radiology*, *55*, 247–249.

DEWANJEE, M. K., 1984. Cardiac and vascular imaging with labelled platelets and leucocytes. *Seminar in Nuclear Medicine*, *14*, 154–187.

DEWANJEE, M. K., CHOWDURY, S. & BROWN, M. L., 1984. Identification of abscesses and thrombi by imaging with 111-In-labelled blood cells. *Mayo Clinic Proceedings*, *59*, 49–50.

DYER, N. H. & DAWSON, A. M., 1970. Diagnosis of Crohn's disease: a continuing source of error. *British Medical Journal*, *i*, 735–737.

ELLIOTT, P. R., LENNARD-JONES, J. E., BARTRAM, C. I., SWAEBRICK, E. T., WILLIAMS, C. R., THOMAS, B. M., DAWSON, A. M. & MORSON, B. C., 1982. Colonoscopic diagnosis of minimal change colitis in patients with a normal barium enema. *Lancet*, *i*, 650–652.

FRICK, M. P., HENKE, C. E., FORSTROM, L. A., SIMMONS, R. A., McCULLOGH, J. & LOKEN, M. K., 1979. Use of 111-In labelled leukocytes in the evaluation of renal transplant rejection: a preliminary report. *Clinical Nuclear Medicine*, *4*, 24–25.

FROELICH, J. W. & SWANSON, D., 1984. Imaging inflammatory processes with labelled cells. *Seminar in Nuclear Medicine*, *14*, 128–140.

KINGHAM, J. G., LEVISON, D. A., BALL, J. A. & DAWSON, A. M., 1982. Microscopic colitis—a cause of chronic watery diarrhoea. *British Medical Journal*, *285*, 1601–1604.

KIPPER, M. S. & WILLIAMS, R. J., 1982. The potential role of In-111-white blood cells scans in patients with inflammatory bowel disease. *Clinical Nuclear Medicine*, *7*, 469–471.

KISSANE, J. M., 1985. *Anderson's Pathology* (C. V. Mosby, St Louis), p. 1082.

KNOCHEL, J. Q., KOEHLER, P. R., LEE, T. G. & WELCH, D. M., 1980. Diagnosis of abdominal abscesses with computer tomography, ultrasound and ^{111}In leukocyte scans. *Radiology*, *137*, 425–432.

McDOUGALL, I. R., BAUMERT, J. E. & LANTIERI, R. L., 1979. Evaluation of ^{111}indium leukocyte whole-body scanning. *American Journal of Roentgenology*, *133*, 849–854.

PETERS, A. M., SAVERYMUTTU, S. H., REAVY, H. J., DANPURE, H. J., OSMAN, S. & LAVENDER, J. P., 1983. Imaging of inflammation with 111-In labelled tropolonate labelled leukocytes. *Journal of Nuclear Medicine*, *24*, 212–216.

SAVERYMUTTU, S. H., CROFTON, M. E., PETERS, A. M. & LAVENDER, J. P., 1983a. Indium-111 tropolonate leucocyte scanning in the detection of intra-abdominal abscesses. *Clinical Radiology*, *34*, 593–596.

SAVERYMUTTU, S. H., LAVENDER, J. P., HODGSON, H. J. F. & CHADWICK, V. S., 1983b. Assessment of disease activity in inflammatory bowel disease: a new approach using ^{111}In granulocyte scanning. *British Medical Journal*, *287*, 1751–1753.

SAVERYMUTTU, S. H., PETERS, A. M., CROFTON, M. E., REES, H., LAVENDER, J. P., HODGSON, H. J. F. & CHADWICK, V. S., 1985. ^{111}Indium autologous leucocyte scanning in the detection of inflammatory bowel disease. *Gut*, *26*, 955–960.

SAVERYMUTTU, S. H., PETERS, A. M., HODGSON, H. J. F., CHADWICK, V. S. & LAVENDER, J. P., 1982. Indium-111 autologous leucocyte scanning: comparison with radiology for imaging the colon in inflammatory bowel disease. *British Medical Journal*, *285*, 255–257.

SAVERYMUTTU, S. H., PETERS, A. M., LAVENDER, J. P., HODGSON, H. J. F. & CHADWICK, V. S., 1983c. ^{111}Indium autologous leucocytes in inflammatory bowel disease. *Gut*, *24*, 293–299.

SAVERYMUTTU, S. H., PETERS, A. M., REAVY, H. J. & LAVENDER, J. P., 1983d. Measurement of granulocyte migration and accumulation in man. *Clinical Experimental Immunology, 52,* 607–612.

SEGAL, A. W., ARNOT, R. N., THAKUR, M. L. & LAVENDER, J. P., 1976. Indium-111-labelled leukocytes for localisation of abscesses. *Lancet, ii,* 1056–1058.

SEGAL, A. W., ENSELL, J., MUNRO, J. M. & SARNER, M., 1980 Indium-111 tagged leucocytes in the diagnosis of inflammatory bowel disease *Lancet, ii,* 230–232.

SFAKIANAKIS, G. N., MNAYMNEH, W., CHANDURMNAY, L., AL-SHEIKH, W., HOURANI, M. & HEAL, L., 1982 Positive In-111 leukocyte scintigraphy in a skeletal metastasis. *American Journal of Roentgenology, 139,* 601–603.

STEIN, D. T., GRAY, G. M., GREGORY, P. B., ANDERSON, M., GOODWIN, D. A. & McDOUGALL, I. R., 1983. Location and activity of ulcerative and Crohn's colitis by ^{111}indium-111 leucocyte scanning. *Gastroenterology, 84,* 388–393.

THOMPSON, W. G., 1984. Gastrointestinal symptoms in the irritable bowel compared with peptic ulcer and inflammatory bowel disease. *Gut, 25,* 1089–1093.

WING, V. W., VON SONNENBERG, E., KIPPER, S. & BIEBERSTEIN, M. P., 1984. Indium-111 labelled leukocyte localisation in haematomas: a pitfall in abscess detection. *Radiology, 152,* 173–176.

Book reviews

The Dosimetry of Ionizing Radiation, Vol. 1. Ed. by K. R. Kase, B. E. Bjärngard and F. H. Attix, pp. x+406+index, 1985 (Academic Press, London), Hardback £60.50, Paperback £31
ISBN 0-12-400401-6 (hardback)
0-12-392651-3 (paperback)

This is the first volume of a new comprehensive treatise on all aspects of radiation dosimetry which will take the place of the existing standard work, first published by Academic Press in 1956. The editors for the new treatise are Kase, Bjärngard and Attix, the last-named having been leading editor of the second edition, so this provides for continuity as well as innovation.

This book begins with a chapter by Carlsson on the theoretical basis for dosimetry which includes a good discussion of the energy quantities involved and of the special radiometric quantities. Kellerer has contributed an extensive chapter on the fundamentals of microdosimetry, a subject which he and Rossi founded and have continued to develop. Dutreix and Bridier write on the dosimetry of external beams of photons and electrons, while Broerse, Lyman and Zoetelief discuss the special problems of the dosimetry of heavy particles. There is then a chapter by Liden and Holm on the measurement of environmental radioactivity and a final one, by Johnson, on internal dosimetry for radiation protection.

The authors' names would be sufficient guarantee for the quality of their contributions and they have, indeed, taken trouble to make this volume a worthy successor to the earlier book. Each chapter is self-contained but there is little or no unnecessary overlap, so the editors have given effective guidance The older, basic literature is not neglected but references from the '80s are numerous and the impression of the whole volume is that it gives very good coverage of the present state of the art. It is of interest to note that Anglo-Saxons no longer dominate the subject. Among the 10 authors of the six chapters there are only two from North America.

The typography is clear and elegant and the binding, at least of the hardback edition, strong enough to survive many years of hard use. Alas, the price is high, but the publishers are to be congratulated on also producing a paperback edition at about half the price, which will tempt workers in the field to add this book to their personal library.

J. W. Boag

DRGs for the Radiologist. Their Meaning and Impact. By R. T. Weiner and R. P. Caterinicchio, pp. x+111, 1985 (John Wiley & Sons Ltd, Chichester), £17.95
ISBN 0-943432-41-3

DRGs are "diagnosis related groups" which have been developed in the United States in response to the need to determine in advance the price per case admitted to hospital for later Federal reimbursement. In the past the Federal Government has met the cost of services "without regard for the legitimacy of those costs".This prospective payment system is a revolutionary reversal of the traditional method by which inpatient hospital care has been financed. These changes have thrown a novel task and responsibility upon hospital management in the United States. It has also changed the role of the radiologist away from simply responding to demand to a more radical assessment of the cost effectiveness of each termination. Not all those who are implementing the changes are enthusiastic supporters. The initials DRG are held by many to stand for "De Revenue's Gone". This little volume, economically presented in soft covers, will be of great interest to American readers.

The technique of considering patients within diagnosis related groups has considerable value for management within the British National Health Service. However, because the National Health Service is cash limited and not funded for each treatment episode it is not possible to transfer the whole philosophy unchanged across the Atlantic. The calculations within a National Health Service must be made from an inverse direction to allocate funds from within a pre-fixed total.

The authors also, quite naturally, concentrate on the impact of the system on radiological practice in the United States. The volume, therefore, is of limited value for British readers and will only be appreciated by the enthusiast. It cannot be recommended for wide readership in this country.

John Roylance

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Radiation dosimetry considerations in the treatment of cystic suprasellar neoplasms*

By E. L. McGuire, M.S., S. Balachandran, M.D. and C.M. Boyd, M.D.

John L. McClellan Memorial Veterans Hospital and Department of Radiology, University of Arkansas for Medical Sciences, Little Rock, Arkansas 72205, USA

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ABSTRACT

Methods and results are given to enable the computation of radiation dose as a function of depth in the wall of a suprasellar cyst containing radioactivity. Both β- and γ-emitting nuclides are considered. The methodology considers distribution of the radioactivity on the cyst wall (spherical shell geometry) and distribution uniformly in the fluid (volume geometry).

Introduction of radioactive colloids into non-resectable cystic suprasellar neoplasms as a treatment modality has been reported previously (Wycis et al, 1954; Lindgren & Westberg, 1964; Bond et al, 1965; Leksell et al, 1967; Backlund et al, 1972; Backlund, 1973; Kobayashi et al, 1981; Balachandran et al, 1985). This paper describes the dosimetric principles involved as applied to several β- and γ-emitting nuclides with therapeutic potential. Cyst geometry and distribution of the colloid within the cyst are taken into consideration.

METHODS

Technical aspects

Suprasellar cysts typically are roughly spherical in shape (Fig. 1) and lie near the optic nerve. To assure minimal irradiation of critical surrounding tissue, a fairly precise dosimetry is indicated. One wishes to determine the dose to the wall of the cyst as a function of depth. The wall thickness is typically about 3 mm. The colloid has previously been found to be distributed with a large fraction attached to the wall of the cyst and the remainder distributed inside the cyst fluid (Balachandran et al, 1985). Other investigators have also noted the attachment to the inner surface of the cyst (Wycis et al, 1954; Bond et al, 1965).

In dosimetry calculations other technical and clinical items of importance are:

(a) accurate radioassay of the radiopharmaceutical prior to administration and to account for the residue after treatment;
(b) imaging of the patient's skull after administration (Balachandran et al, 1985) to determine the actual amount incorporated in the cyst, extracystic tissue and decompression reservoirs; and
(c) determination of cyst-wall thickness and cyst volume by an appropriate imaging modality (computed tomography (CT) or magnetic resonance imaging).

Dosimetry principles

General. Radiation dose to the cyst wall arises from the activity distributed on the inner surface of the cyst and that mixed in the cyst fluid. The nuclide considered may emit β and/or γ radiation. The ideal nuclide,

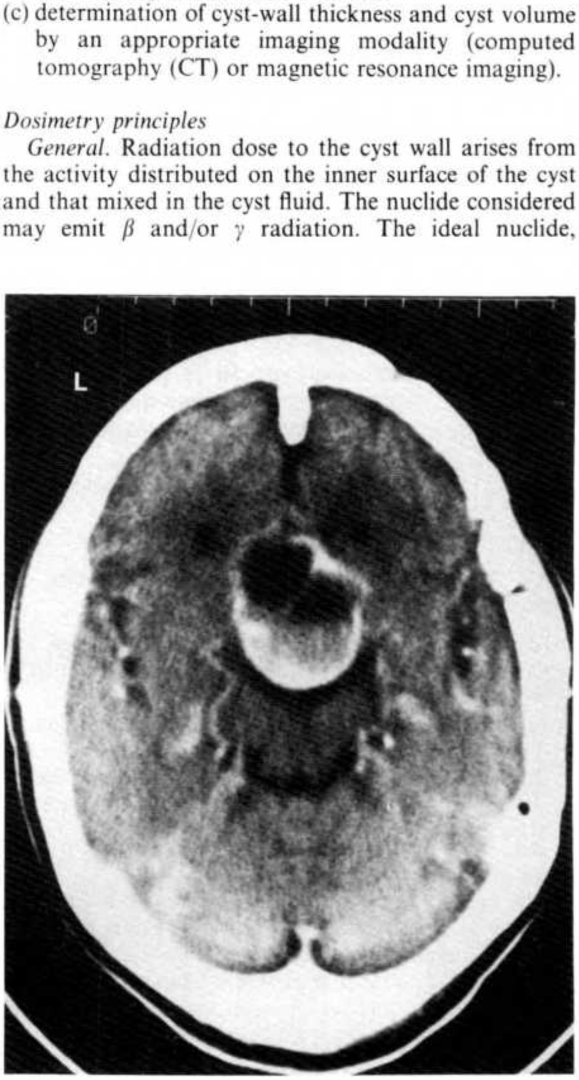

FIG. 1.

Contrast-enhanced CT scan of the head showing a cystic neoplasm in the sella turcica.

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*This paper reflects the views of the authors and does not necessarily reflect the policies or procedures of the Veterans Administration Medical Center.

though, would intuitively appear to be a pure β-emitter with a high energy and a relatively short half-life. The dose delivered to surrounding tissue should be low. In this investigation the nuclides chosen were ^{32}P, ^{90}Y and ^{198}Au, which have previously been used for this treatment, and ^{131}I and ^{24}Na were included to investigate the effects of medium- to high-energy γ and β particles on depth dose.

Calculations. The symbols used in the following equations are:

$F_\beta(x, x_{90})$ = β particle scaled absorbed dose distribution
$B_{ea}(\mu x)$ = energy absorption build-up factor
$R(x)$ = dose-rate at a distance x cm (Gy/s (100 rad/s))
R_∞ = dose computed to infinite decay time
μ = linear energy absorption coefficient (cm^{-1})
μ_{ea}/ρ = mass energy absorption coefficient (cm^2/g)
ρ = density of medium, assumed to be unity in calculations (g/cm^3)
S_A or S_V = source activity in units of 3.7×10^4 Bq/cm^2 (3.7×10^4 dis/s/cm^2), S_A or 3.7×10^4 Bq/cm^3 (3.7×10^4 dis/s/cm^3), S_V
x_{90} = β particle distance for 90% absorption (cm)
n = number of particles or photons emitted per nuclear transformation
E_γ or $\bar{E}_\beta$ = energy (MeV) of γ radiation, mean energy (MeV) of β radiation
k = constant, energy to dose conversion, 1.6×10^{-10} g Gy/MeV (1.6×10^{-8} g rad/MeV)

Dose calculations for the following situations are described:

(a) depth dose from a uniform activity of 3.7×10^4 Bq/cm^2 (1 μCi/cm^2) on the interior of a spherical shell; and
(b) dose from a uniform activity of 3.7×10^4 Bq/cm^3 (1 μCi/cm^3) contained inside a spherical volume. The medium inside and outside the sphere is assumed to be comprised of the same tissue-equivalent material.

Beta and photon emitters are considered for both cases (a) and (b).

The spatial description of the dose from extended (volume or area) source geometries is given in several standard radiation dosimetry and shielding references (Blizard, 1962; Blizard et al, 1968; Chilton et al, 1984). For extended photon sources, the point kernel described by:

$$G(x)_\gamma = [\exp(-\mu x)/4\pi x^2] \cdot B_{ea}(\mu x) \cdot \mu_{ea}/\rho$$

is integrated with the source geometry considered. These integrals cannot always be evaluated analytically but for some simple geometries they can be integrated numerically with the aid of a computer.

TABLE I

PHYSICAL CHARACTERISTICS OF NUCLIDES CONSIDERED

Nuclide	Half-life (h)	$\bar{E}_\beta$ (MeV)	E_γ (MeV)	n
^{24}Na	15	0.555		1.0
			1.37	1.0
			2.75	1.0
^{32}P	343	0.69		1.0
^{90}Y	64	0.94		1.0
^{131}I	193	0.183		1.0
			0.364	0.82
			0.080	0.0258
			0.284	0.0578
			0.637	0.0653
			0.723	0.0173
			0.030	0.037
^{198}Au	64.7	0.316		1.0
			0.4117	0.955
			0.6758	0.0107
			0.070	0.02

The treatment and application of β point kernals are described by Berger (1970, 1971) and the integrals over various source geometries are treated in a similar fashion as the γ point kernels.

Doses were computed at depths of interest for an initial dose-rate $R(z)$ and the dose due to total decay,

$$R_\infty = R(z)\int_0^\infty \exp(-\lambda t)\mathrm{d}t.$$

The physical parameters of the nuclides considered are given in Table I (Dillman & Von der Lage, 1975).

Spherical shell source: beta-emitters

The geometry of a spherical shell source is closer to the physical situation than the plane source geometry given previously (Balachandran et al, 1985).

The dose-rate at z from the surface of a spherical shell of radius r is:

$$R_s(z,\beta) = 2\pi\, S_A n k \bar{E}_\beta (r/r+z)\int_z^{z+2r} x\, G(x)_\beta\, \mathrm{d}x \quad (1)$$

(Chilton et al, 1984; Blizard et al, 1968).

The β point kernel $G(x)_\beta$ may be formulated as:

$$G(x)_\beta = F_\beta(x/x_{90})/4\pi\rho x^2 x_{90}$$

(Berger, 1971).

We may write Equation (1) for β emitters then as:

$$R_s(z,\beta) = (S_A n k \bar{E}_\beta/2\rho x_{90})(r/r+z)\int_z^{z+2r} F_\beta(x/x_{90})/x\,\mathrm{d}x \quad (2)$$

Tabulations of the β point kernel for various nuclides are given in the same reference. For the evaluation of the integral in Equation (2), $F_\beta(x/x_{90})$ was written in terms of a polynomial as:

$$F_\beta(x/x_{90}) = \sum_{i=0}^{4} a_i x^i,$$

for each of the β-emitting nuclides.

Spherical shell source: photon-emitters

Similarly to Equation (1) for β-emitters, for γ-emitters in a spherical shell geometry:

$$R_s(z, \beta) = 2\pi\, S_A nkE_\gamma(r/r+z) \int_z^{z+2r} x\, G(x)_\gamma \mathrm{d}x \qquad (3)$$

where $G(x)_\gamma$, the point kernel for γ-emitters is·

$$G(x)_\gamma = \exp(-\mu x)/4\pi x^2 \cdot B_{en}(\mu x) \cdot \mu_{en}/\rho$$

(Berger, 1968).
The mass energy absorption coefficient μ_{en}/ρ was taken from Hubbell (1977). The build-up factor $B_{en}(\mu x)$ can be written as

$$B_{en}(\mu x) = 1 + a\mu x \exp(b\mu x),$$

(Chilton, et al, 1984),
where the constants a and b are tabulated in Chilton et al (1984) Thus, Equation (3) can be written:

$$R_s(z, \gamma) = (S_A nkE_\gamma/2) \cdot \mu_{en}/\rho\,(r/r+z)$$
$$\int_z^{z+2r} \{\exp(-\mu x)/x + a\mu \exp[\mu x(b-1)]\}\mathrm{d}x \qquad (4)$$

Spherical volume source: beta-emitters

For a spherical volume source in which the activity is distributed uniformly inside the sphere, the dose-rate at a distance z from a sphere of radius r is:

$$R_V(z, \beta) = S_V nk\bar{E}_\beta \int_0^\infty x^2\, \psi(x) b(x)_\beta \,\mathrm{d}x \qquad (5)$$

(Berger, 1970),
where $\psi(x)$ is the geometric reduction factor as discussed in Berger (1970). For a point of interest outside the sphere ($z > r$):

$$\psi(x) = \begin{array}{ll} 0 & (0 < x < z-r) \\ r-(x-z)/4xz & (z-r < x < z+r) \\ 0 & (z+r < x) \end{array}$$

$G(x)_\beta$ as previously described is then inserted into Equation (5) and the resultant equation is then integrated numerically.

Spherical volume source: photon-emitters

The method used to evaluate the dose-rate at a point outside a sphere containing a uniform distribution of activity has been adapted from Ono & Tsuruo (1965).

The geometry and attenuation media considered are a γ-emitter uniformly distributed in a sphere (radius R) composed of aqueous material with the attenuation medium outside the sphere identical to that inside. The dose is computed at a point a distance z from the surface of the sphere. We may then write for the dose outside the sphere:

$$R(x) = T \int_V \exp(-\mu x)/4\pi x^2 B_{en}(\mu x)\,\mathrm{d}V \qquad (6)$$

where $T = S_V nkE_\gamma(\mu_{en}/\rho)$, $x = z+R$, and $B_{en}(\mu x)$ is as previously given. Using geometrical relationships and r, ϕ and ψ as variables of integration as shown in Ono and Tsuruo (1965), we can write Equation (6) as:

$$R(x) = T/4\pi \int_0^{2\pi}\int_0^{\phi_0}\int_{r_2}^{r_1} \frac{x^2 \exp(-\mu r \sec\phi)}{x^2} B_{en}(\mu x) \sin\phi \sec\phi \,\mathrm{d}r\,\mathrm{d}\phi\,\mathrm{d}\psi$$
$$= T/2 \int_0^{\phi_0}\int_{r_2}^{r_1} \exp(-\mu r \sec\phi)\, B_{en}(\mu x) \tan\phi \,\mathrm{d}r\,\mathrm{d}\phi$$
$$= T/2\mu \int_0^{\phi_0} [\exp(-\mu r_1 \sec\phi) - \exp(-\mu r_2 \sec\phi)]\, B_{en}(\mu x) \sin\phi \,\mathrm{d}\phi \qquad (7)$$

Equation (7) was then integrated numerically using Simpson's rule.

RESULTS

Doses at depths up to 4.6 mm outside the sphere were computed for the nuclides mentioned for sphere volumes of 1, 5, 10, 20, 50, and 100 cm³.

For the β spherical shell geometry there was little difference in the dose at depth as a function of sphere volume for the nuclides considered. Figure 2 presents this relationship, which holds for all the nuclides, suggesting there is no energy dependence. Figures 3 and 4 give the numerical results of the dose calculations for both $R_s(z, \beta)$ and R_∞ using Equation (2). A sphere volume of 20 cm³ and a uniform distribution of 3.7×10^4 Bq/cm² (1 μCi/cm²) was assumed.

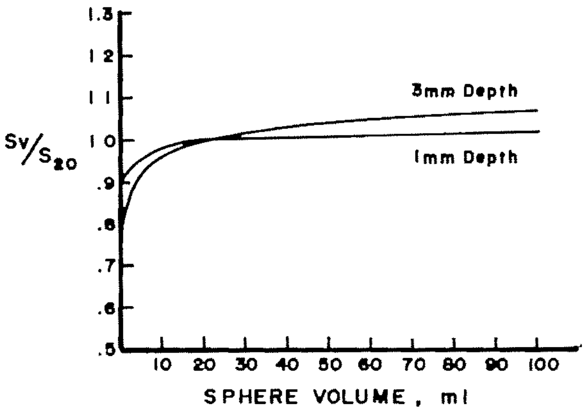

FIG. 2.

β dose at depth dependence on volume of sphere for spherical shell geometry. Dose ratio is for sphere volume stated (S_V) to 20 cm³ sphere (S_{20}).

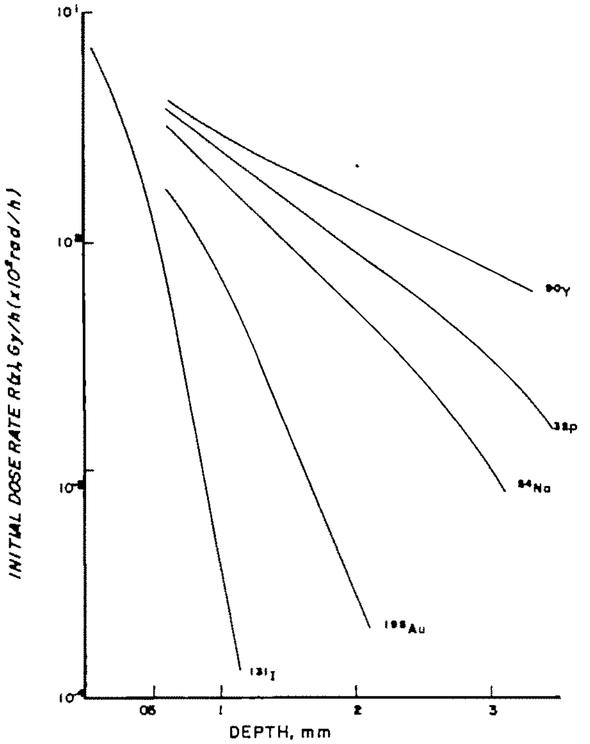

Fig. 3.

Initial β dose-rate at various depths around a spherical source of 20 cm³ with an activity of 3.7×10^4 Bq/cm² (1 μCi/cm²) uniformly distributed on wall of sphere (spherical shell geometry)

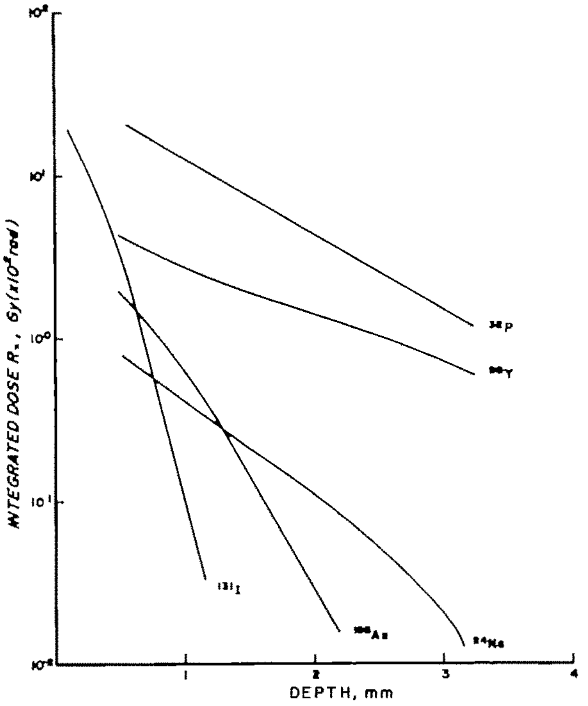

Fig. 4.

Integrated β dose at various depths around a spherical source of 20 cm³ with an activity of 3.7×10^4 Bq/cm² (1 μCi/cm²) uniformly distributed on wall of sphere (spherical shell geometry).

Figure 5 summarises the results of the sum of the doses computed for both β and γ emissions from each nuclide, if applicable. The "flattening out" of the curves at increasing distance for ^{198}Au, ^{131}I and ^{24}Na represents the contribution from the γ emissions. The photons contribute a relatively high component of the dose at small distances. For ^{24}Na and ^{198}Au the dose from the β particles exceeded that due to the γ emissions only at depths less than about 2 mm for the spherical shell geometry. For ^{131}I the γ dose exceeded the β dose at all depths greater than about 0.5 mm.

It was found that the dose contribution from a uniform activity in the sphere volume (S_V) for β and γ emitters was a small fraction of that contribution from the activity on the wall of the sphere. For ^{32}P and ^{90}Y, this fraction was less than 10% for 1 mm and 3 mm depths. Figure 5 shows results of the other nuclides for the spherical volume geometry. For the γ-emitting nuclides, there was less of a difference between the geometries, although the volume/shell fraction at distances less than 3 mm remained less than 0.25. Figure 6 shows the doses delivered at depth for the spherical shell geometry, with the activity normalised to deliver 100 Gy (10 krad) at 3.0 mm. The γ contribution becomes more pronounced at depths greater than 3 0 mm, as is shown. It may be seen that ^{90}Y gives a higher dose than ^{32}P at depths greater than 3.0 mm, which may be a consideration when dose to surrounding tissue is of concern. However, if the total dose must be delivered in a short period of time, ^{90}Y might be the nuclide of choice; ^{90}Y delivers 90% of its total dose in 9 days while ^{32}P, for example, delivers 90% of its total dose in 45 days.

Discussion

Previous reports in the literature of the radiocolloid treatment of cysts (Wycis et al, 1954, Bond et al, 1965; Leksell et al, 1967; Backlund et al, 1972; Kobayashi et al, 1981) have treated the dose calculations less rigorously than in this paper. The previous reports usually discussed the dose at the inner surface of the cyst rather than the dose at depth in the cyst wall and surrounding tissue, as given in this paper. Further, the computational methods used and the lack of nuclide distribution information generally given make it difficult to compare the present results with the previous reports. Results of the previous studies which can be directly compared with this study are summarised in Table II.

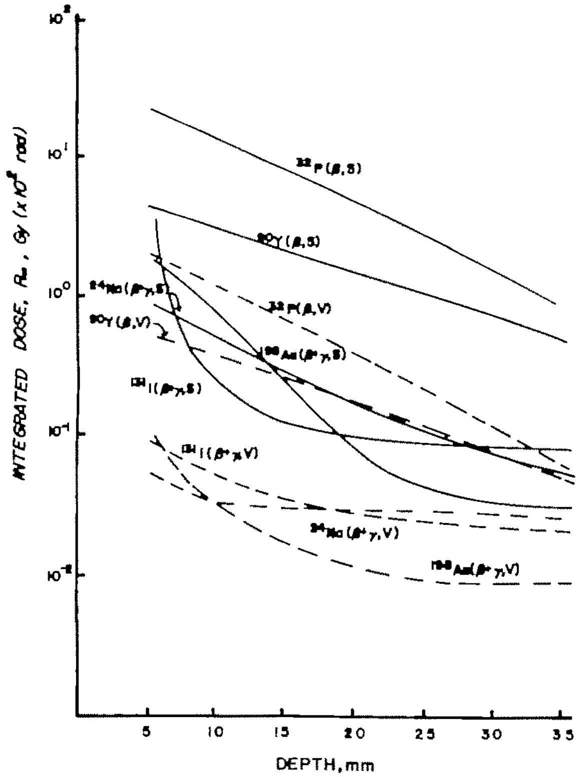

FIG. 5.

β and γ integrated doses at depth for spherical shell (s) geometry and volume (v) geometry.

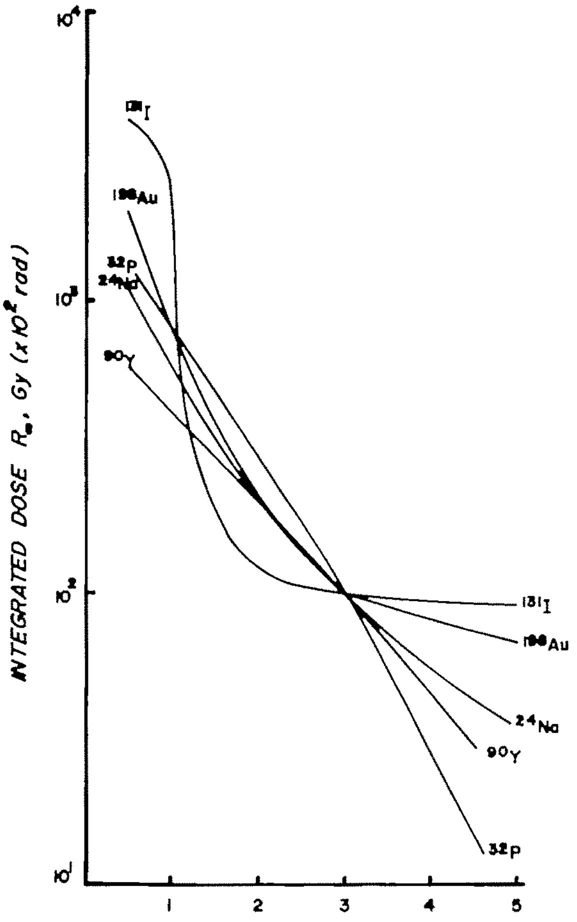

FIG. 6.

β and γ integrated doses at depth for spherical shell geometry. Activity normalised to give 100 Gy (10 krad) at 3.0 mm depth

Wycis et al (1954) computed doses for ^{32}P using both a spherical shell geometry and a volume source geometry. For the spherical shell, doses were given as the total energy absorbed in a shell of 7 mm radius (the stated range of the β particle), at the inner surface of the cyst wall, and at 1.7 mm (the stated half-value thickness) in the cyst wall. The cyst volume considered was 11 cm³. For the limited number of results presented, their values compare reasonably well with our results. Wycis et al assumed that some of the colloid was attached to the wall of the cyst and some remained in the fluid, an assumption which is supported by Balachandran et al (1985) and Bond et al (1965). Leksell et al (1967) and Backlund et al (1972), using ^{32}P and ^{90}Y, assumed the volume distribution only, and computed the dose to the inner surface of the cyst wall by the use of the formula:

$$D_C = (73.8)(f)\,(\bar{E}_\beta)\,(T_{eff})(A/V),$$

where D_C = dose to the inner surface of the cyst (rad), 73.8 = constant (3.2×10^9 dis/day/ μCi $\times 1.44 \times 1.6 \times 10^{-8}$ g rad/MeV), f = volume-dependent constant representing the fraction of the dose at the inner surface compared with the total dose absorbed, $\bar{E}_\beta$ = average energy (MeV), T_{eff} = effective half-life (days), and $(A/V) = \mu$Ci/g. These authors also gave the dose outside the sphere for both ^{32}P and ^{90}Y using an undescribed methodology. The agreement with our results ranges from a slight underestimate for ^{32}P to an overestimate by a factor of 4 for ^{90}Y.

Bond et al used ^{198}Au in their studies and assumed the volumetric distribution for their dose estimates. They assumed that all the β dose would be absorbed in the cyst wall and the dose at 1 cm beyond the cyst would be entirely due to the γ radiation. Their computed value for this instance compares poorly with our value. In their patient treatments, they used from 1.11×10^9 to 1.11×10^{10} Bq (30–300 mCi) of ^{198}Au. In an effort to explain some of their clinical results which showed unexpectedly high radiation effects, they noted that some of the ^{198}Au compound tended to acculumate on the lining of the cyst wall. Results of this paper for

TABLE II

COMPARISON OF DOSIMETRY RESULTS OF PRESENT STUDY WITH PREVIOUS STUDIES

Reference	Depth (mm)	Nuclide distribution			
		^{32}P		^{90}Y	^{198}Au
		S_A	S_V	S_V	S_V
Wycis et al (1954)	1.7	2*E*–4 (1.6*E*–4)			
	0.6		4.6*E*–5 (5.1*E*–5)		
Leksell et al (1967) and Backlund et al (1972)	1.0		1.35*E*–5 (3.2*E*–5)	4.05*E*–5 (9.7*E*–6)	
	3.0		2.7*E*–6 (3.0*E*–6)	1.35*E*–6 (2.1*E*–6)	
Bond et al (1965)	10				2.2*E*–7 (<5.4*E*–8)

Values given are doses in Gy/3.7×10^4 Bq/cm^2, (S_A) or Gy/3.7×10^4 Bq/cm^3 (S_V), as appropriate. Present study results given in parentheses

the spherical shell distribution give a dose of 700 Gy (70 000 rad) at 1 mm and 40 Gy (4000 rad) at 3 mm for a 4 cm diameter cyst containing 3.7×10^9 Bq (100 mCi) of ^{198}Au. Our calculations indicate this dose is almost entirely due to the β radiation at 1 mm and γ radiation at depths greater than 2 mm (see Fig. 4 for the β contribution and Fig 5 for the $\beta+\gamma$ contribution).

Kobayashi et al (1981) assumed a volume distribution only and used ^{198}Au and ^{32}P. These authors give a formula with which dose outside the cyst may be computed, but the formula does not contain the geometric reduction factor discussed by Berger (1970). They also state that in some of their therapy cases, an earlier β point kernel (Loevinger et al, 1956) was used for the dose calculations. Cyst volumes, activity administered, cyst-wall thickness, and cyst-wall radiation dose are given in their case summary table. However, at what depth this dose is computed is uncertain, as is the methodology used. Thus, their results cannot be directly compared with the results of the present work.

In this paper, we have given figures summarising the results of the dose calculations. Figures 3–6 may be useful for estimating doses of a particular radionuclide needed to produce a chosen radiation dose and the expected dosimetry at depth beyond the cyst.

Since colloids are usually distributed primarily on the cyst-wall surface, the spherical shell geometry is the most applicable dosimetric method in the usual clinical situation (*e.g.* intracranial cysts). Thus, Fig. 6 may be used for most situations to prescribe an activity for a known cyst size.

Other findings of this study include:

(a) for the spherical shell geometry, the dose-rate was found to depend only weakly on sphere size;

(b) the results suggest that pure β-emitters only should be considered for this treatment. Photon-emitters contribute an appreciable dose at the depths considered and obviously irradiate adjacent tissue (at depths greater than the β particle range) more than the β-emitters, and

(c) the findings suggest, for the nuclides and parameters considered, that ^{32}P would be the optimum nuclide since, for a given dose and depth, it would deliver a greater dose at depths less than the given depth, and deliver a smaller dose to surrounding tissue for a given total integrated depth dose compared with the other nuclides.

The actual radiation dose needed to cause a desired effect is still unknown. Future studies are needed, and these results may be used to provide a basis for a more rigorous dosimetry in treatment of cases of this nature.

REFERENCES

BACKLUND, E. O., 1973. Studies on craniopharyngiomas. *Acta Chirurgica Scandinavica, 139,* 237–247.

BACKLUND, E. O., JOHANSSON, L. & SARBY, B., 1972. Studies on craniopharyngiomas *Acta Chirurgica Scandinavica, 138,* 749–759.

BALACHANDRAN, S., MCGUIRE, E L., FLANIGAN, S., SHAH, H & BOYD, C. M., 1985 Bremmstrahlung imaging after ^{32}P treatment for residual suprasellar cyst. *International Journal of Nuclear Medicine and Biology, 12,* 215–221

BERGER, M J, 1968 *Energy Deposition in Water by Photons from Point Isotropic Sources.* NM/MIRD Pamphlet No 2 (Society of Nuclear Medicine, New York)

BERGER, M. J., 1970 Beta-ray dosimetry calculations with the use of point kernels In *Medical Radionuclides Radiation Dose and Effects.* Ed. by R. J. Cloutier, C L. Edwards & W. S. Snyder (CONF-69212, NTIS, Springfield, Va)

BERGER, M. J., 1971. *Distribution of Absorbed Dose Around*

Point Sources of Electrons and Beta Particles in Water and Other Media. NM/MIRD Pamphlet No. 7 (Society of Nuclear Medicine, New York).

BLIZARD, E. P., 1962. Analytical methods of shield design. In *Reactor Handbook,* Volume III, Part B, *Shielding.* Ed. by E. P. Blizard (Interscience Publishers, New York), pp. 128–150.

BLIZARD, E. P., FODERARO, A., GOUSSEV, N. G. & KOVALEV, E. E., 1968. Extended radiation sources (point kernel integrations). In *Engineering Compendium on Radiation Shielding.* Ed. by R. G. Jaeger, E. P. Blizard, M. Grotenhuis, A. Honig, Th. A. Jaeger & H. H. Eisenlohr (Springer-Verlag, New York), pp. 363–416.

BOND, W. H., RICHARDS, D. & TURNER, E., 1965. Experiences with radioactive gold in the treatment of craniopharyngioma. *Journal of Neurology, Neurosurgery and Psychiatry, 28,* 30–38.

CHILTON, A. B., SHULTIS, J. K. & FAW, R. E., 1984. *Principles of Radiation Shielding* (Prentice Hall, Englewood Cliffs, New Jersey).

DILLMAN, L. T. & VON DER LAGE, F. C., 1975. *Radionuclide Decay Schemes and Nuclear Parameters for Use in Radiation Dose Estimation.* NM/MIRD Pamphlet No. 10 (Society of Nuclear Medicine, New York).

HUBBELL, J. H., 1977. Photon mass attenuation and mass energy absorption coefficients for H, C, N, O, Ar, and seven mixtures from 0.1 keV to 20 MeV. *Radiation Research, 70,* 58–81.

KOBAYASHI, T., KAGEYAMA, N. & OHARA, K., 1981. Internal irradiation for cystic craniopharyngioma. *Journal of Neurosurgery, 55,* 896–903.

LEKSELL, L., BACKLUND, E. O. & JOHANSSON, L., 1967. Treatment of craniopharyngiomas. *Acta Chirurgica Scandinavica, 133,* 345–350.

LINDGREN, E. & WESTBERG, G., 1964. Radioactive bismuth phosphate for the treatment of craniopharyngioma. *Acta Radiologica Therapy, 2,* 113–120.

LOEVINGER, R., TAPHA, E. M. & BROWNELL, G. L., 1956. Discrete radioisotope sources. In *Radiation Dosimetry.* Ed. by G. J. Hine & G. L. Brownell (Academic Press, New York), pp. 694–799.

ONO, H. & TSURUO, A., 1965. An approximate calculation method of flux for spherical and cylindrical sources with a slab shield. *Journal of Nuclear Science and Technology, 2,* 229–235.

WYCIS, H. T., ROBBINS, R., SPIEGEL-ADOLF, M., MESZAROS, J. & SPIEGEL, E. A., 1954. Studies in stereoecephalotomy III. *Confinia Neurologica, 14,* 193–202.

Book reviews

Environmental Health Criteria 46 Guidelines for the Study of Genetic Effects in Human Populations. WHO, pp. 126, 1985 (WHO, Geneva), Sw.Fr. 12
ISBN 92-4-150186-5

The International Programme on Chemical Safety (IPCS) is jointly sponsored by the World Health Organization, the International Labour Office and the United Nations Environment Programme It was founded in response to the realisation that there was, and still is, an urgent need to identify hazardous environmental chemicals and to assess their effects on the health of the human population, these being prerequisites to devising effective control measures

As a means of promoting the safe use of chemicals the IPCS has published a series of *Environmental Health Criteria* covering compounds such as DDT, styrene, epichlorhydrin, and many others This book, the 46th in the series, is different from most of its predecessors in that it does not deal with any one compound or class of compunds. Instead it suggests guidelines for the design and execution of genetic studies on human populations exposed, or suspected of being exposed, to mutagenic agents. The contributors are all experts in their fields.

The book begins with a consideration of methodological and epidemiological issues. Thereafter it falls into two main sections dealing separately with mutations in somatic cells and germinal mutations. Detailed procedures are not included. Instead those matters which should be considered when setting up a study are discussed in more general terms. Pitfalls to be avoided are also pointed out. For the most part only well established test systems are included.

These guidelines would serve as a good starting point for anyone new to the assessment of human genetic hazards and will provide worthwhile cautions to those already engaged in the subject.

ROBERT DEWDNEY

SI Units in Radiation Protection and Measurements. NCRP Report No. 82, pp. vi+64, 1985 (NCRP, Bethesda, Maryland), $10.00.
ISBN 0-913392-74-X

In our ever more technological society it is essential that scientists should agree on an international language of measurement so that they can communicate without impediment not only with each other but also, even more importantly, with the intelligent layman. Nowhere is this more important than in radiation protection, which depends crucially on the objective, quantitative assessment and control of radiation fields. Although there is much public concern about radiation hazards, discussion is often bedevilled by failure to come to grips with numbers, even with orders of magnitude. So worry, confusion and prejudice reign supreme

The relevant physical concepts have been clearly defined, but there is reluctance, only too understandably, to discard the old ways and to adopt finally the only system of measurement that can possibly command universal acceptance, Le Système International d'Unités

This NCRP report commences with a cogent account of the SI system, followed by persuasive illustrations of its advantages in radiation science, protection, radiation therapy, diagnostic radiology and nuclear medicine. Though there are in the US, as elsewhere, commercial pressures favouring the status quo, "the cost of switching (to the SI) in the near future will be less than the cost of switching at any later time". The need for regulatory amendments is recognised and governmental co-operation is regarded as both "essential" and "feasible". Accordingly, NCRP recommends an immediate start to the adoption of SI units, to be completed by the end of 1989.

Various conversion tables are provided. Let us hope that they will soon become unnecessary.

M. J. DAY

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Technical note

Foamed epoxy resin-based lung substitutes

By D. R. White, Ph.D., C.Phys., F.Inst.P., *C. Constantinou, M.Sc., Ph.D. and †R. J. Martin, B.Sc., A.R.C.S.

Radiation Physics Department, St Bartholomew's Hospital, London EC1A 7BE, *Tufts-New England Medical Center, Medical Physics Division, Boston, Massachusetts 02111, USA and †Ciba-Geigy Plastics, Duxford, Cambridge CB2 4QA

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A variety of materials have been introduced over the years to simulate lung tissue, with both foamed and granulated products being used (Edling, 1944; Alderson et al, 1962; Rogers, 1970; Stacey, 1972; McGinley, 1973; White, 1974; Constantinou, 1978). Unfortunately, many available lung substitutes have imprecise or variable elemental compositions. In addition, complex manufacturing procedures are frequently necessary in order to produce the required material.

In this note a range of foamed lung substitutes based on an epoxy resin system are discussed. The substitutes have well defined elemental compositions and radiation interaction characteristics for photons and electrons that closely match those of the lungs. By careful addition of a special foaming agent, the mass density of the final material may be at any derived value within the quoted mass density range of the inflated/deflated lung (260–1050 kg m^{-3}) (International Commission on Radiological Protection (ICRP), 1975).

It should be noted that the materials presented here use the same foaming agent (Dow Corning, DC1107) as that described by Constantinou (1978) in his Ph.D. Thesis.

MATERIALS

The use of epoxy resin systems in the manufacture of tissue substitutes was discussed in detail by White et al (1977), when 15 substitutes were introduced, including a lung material designated LN4. The formulation LN4 represented the lowest-density material that could be produced at that time by loading the epoxy resin system, CB2, with the low-density filler, phenolic microspheres (PMS). The resulting mass density of 600 kg m^{-3} was higher than the lowest reported density of the inflated lung.

In the present study, the foamed materials were formulated from the following constituents.

Epoxy resin system, CB2M

A modified version of the low viscosity epoxy resin system, CB2 (White et al, 1977) was used with the reactive diluent Epoxide No. 7, now withdrawn, replaced by the chemically similar Epoxide No. 8. The modified system, CB2M, comprised 100 parts by mass Araldite MY 750, 50 parts by mass Epoxide No. 8, an aliphatic monoglycidyl ether containing principally C_{12} and C_{14} alkyl groups, and 28 parts by mass hardener HY 2996 (formally designated XD 555), a mixture of 2,2,4- and 2,4,4-trimethyl-1,6-diaminohexane.

Typical formula (percentage by mass): H(9.53); C(72.69); N(2.79); O(14.74); Cl(0.25).

Mass density: 1080 kg m^{-3}.

Phenolic microspheres, PMS (Type BJO 0930)

A low-density particulate filler used to reduce the density of the epoxy resin-based material making up the solid walls of the foam to a value more appropriate to lung tissue.

Typical formula (percentage by mass): H(7.88); C(78.23); O(13.89).

Mass density: ~ 200 kg m^{-3}.

Polyethylene

A powdered filler (mean particle diameter < 50 μm) used to maintain the required hydrogen content of the final material and to alter the viscosity of the resin/filler mixture.

Typical formula (percentage by mass): H(14.37); C(85.63).

Mass density: 920 kg m^{-3}.

Magnesium oxide

A powdered filler (mean particle size < 100 μm) used as the primary high atomic number constituent for modifying the photon attenuation characteristics of the substitute.

Typical formula (percentage by mass): Mg(60.31); O(39.69).

Mass density: 3580 kg m^{-3}.

Foaming agent, DC1107

This is a polyfunctional cross-linking agent. The functional group is hydrosilane ($\equiv$ Si – H) which reacts with acids, bases, amines, etc., liberating hydrogen. When added to the epoxy resin system, the gas acts as a "blowing agent" producing an aerated structure. Theoretically, the addition of 0.001 kg of DC1107 could release up to 3.6×10^{-4} m^3 of hydrogen gas, assuming normal temperature and pressure. Approximately 1% by mass of DC1107 produces enough hydrogen to "blow" 0.1 kg of resin/filler mixture to more than three times its original volume, producing a mass density ~ 300 kg m^{-3}.

Typical formula (percentage by mass): H(6.90); C(21.43); O(25.64); Si(46.03).

Mass density. 1000 kg m^{-3}.

Surfactant, DC200/50

A liquid component, polydimethylsiloxane, used to alter the surface tension of the resin/filler mixture. This results in a more uniform pore size when the foaming agent, DC1107, is added and the mixture foamed.

Typical formula (percentage by mass): H(8.33); C(33.08); O(20.90); Si(37.69).

Mass density: 960 kg m^{-3}.

Araldite MY 750 and HY 2996 are supplied by Ciba-Geigy Plastics; Epoxide No. 8 is a product of Proctor & Gamble Ltd; PMS(BJO 0930) is a product of Union Carbide Ltd. Fine polyethylene powder (Type HA2578) from Atochem Ltd and reagent grade magnesium oxide from Hopkin & Williams Ltd, were used in this study. The surfactant DC200/50 and the foaming agent DC1107 are produced by Dow Corning Ltd.

THE FORMULATED LUNG SUBSTITUTES

The lung substitutes were formulated (White, 1977) so as to simulate, for photon and electron interactions, the composition of lung suggested by ICRP (1975). The elemental composition (percentage by mass) accepted for lung was: H(9.9); C(10.0); N(2.8); O(74.0); Na(0.18); Mg(0.007); Al(0.001); P(0.08); S(0.22); Cl(0.26); K(0.19); Ca(0.01); Fe(0.04); Zn(0.001).

The mass density range for inflated/deflated lung (ICRP, 1975) is 260–1050 kg m^{-3}.

A group of five representative lung substitutes is given in Table I, which shows the percentage masses of the constituents of each substitute and their descriptive code. Table II gives the elemental composition of each lung substitute and the measured mass density.

In order to assess the radiation simulation properties of the new formulations, photon and electron interaction data have been calculated in the energy interval 10 keV–100 MeV and compared with similar data for lung Mass attenuation coefficients (μ/ρ) and mass energy absorption coefficients (μ_{en}/ρ) were calculated at 33 energies by applying the mixture rule to the elemental cross-sections of Hubbell (1969) and Storm and Israel (1970). Total electron mass stopping powers (S/ρ) were calculated from the data of Berger and Seltzer (1964), Kim (1973) and the International Commission on Radiation Units and Measurements (ICRU, 1984a). Mass scattering powers for electrons (T/ρ) were derived from the mathematical expressions given by ICRU (1984b). Using the densities given in Table II, the maximum and minimum values of the ratios: $\mu_{substitute}/\mu_{lung}$, $(\mu_{en})_{substitute}/(\mu_{en})_{lung}$, $S_{substitute}/S_{lung}$ and $T_{substitute}/T_{lung}$ over the stated energy interval are listed in Table III. It is clear that the ratios are within

TABLE I

THE CONSTITUENTS OF THE NEW LUNG SUBSTITUTES

Constituents	Proportion (percentage by mass)				
	LN10/00	LN10/25	LN10/50	LN10/75	LN10/100
CB2/M	59.65	59.76	59.89	60.00	60.11
Polyethylene	15.00	15.00	15.00	15.00	15.00
MgO	19.77	19.46	19.14	18.83	18.52
PMS	4.58	4.53	4.47	4.42	4.37
DC200/50	1.00	1.00	1.00	1.00	1.00
DC1107	—	0.25	0.50	0.75	1.00

TABLE II

THE ELEMENTAL COMPOSITIONS AND MEASURED MASS DENSITIES OF THE NEW LUNG SUBSTITUTES

Lung substitute	Elemental composition (percentage by mass)							Measured mass density (kg m^{-3})
	C	H	N	O	Mg	Si	Cl	
LN10/00	60.12	8.28	1.66	17.49	11.92	0.38	0.15	1014
LN10/25	60.21	8.31	1.67	17.43	11.74	0.49	0.15	521
LN10/50	60.32	8.33	1.67	17.38	11.54	0.61	0.15	411
LN10/75	60.41	8.36	1.67	17.33	11.36	0.72	0.15	308
LN10/100	60.50	8.38	1.68	17.28	11.17	0.84	0.15	288

TABLE III

The relative photon and electron interaction characteristics (10 keV–100 MeV) of the new lung substitutes

Lung substitutes	$\mu_{substitute}/\mu_{lung}$	$(\mu_{en})_{substitute}/(\mu_{en})_{lung}$	$S_{substitute}/S_{lung}$	$T_{substitute}/T_{lung}$
LN10/00	0.97–1.02	0.98–1.02	0.98–1.01	0.96
LN10/25				
LN10/50				
LN10/75				
LN10/100				

4% of unity for both photons and electrons and in many instances within 2% of unity.

Manufacturing Procedure

Details of manufacturing foamed lung substitutes, including the use of foaming agents such as DC1107, have been published elsewhere (White & Constantinou, 1982). Consequently, only the brief outline of the procedure is given in this section.

Essentially, the procedure is as follows:

(1) Accurately dispense the required masses of MY 750, Epoxide No. 8, HY 2996, polyethylene, MgO, PMS and DC200/50 (in that order) into a suitable plastic container.
(2) Mix the components well, using an electrically operated mechanical stirrer. This process may be carried out *without* using any evacuation techniques.
(3) Add the required mass of DC1107 and rapidly stir to disperse the liquid. Depending upon such factors as degree of dispersion and temperature of mixture, foaming will commence some 10–15 s after the addition of DC1107.
(4) Pour the mixture into a suitable release-treated mould. It is important to ensure that the two- to three-fold increase in the volume of the mixture will be contained within the mould. The material will gently rise in the mould, hardening to a rigid, machinable foam in 48 h. During the foaming and hardening process, the mixture in the mould should not be disturbed or subjected to mechanical shock.

In the interests of safety, (1)–(4) should be performed in a fume cupboard, although excessive air flow should not be allowed to disturb the formation of the foam.

Discussion

The lung substitutes described here give adequate simulation of lung for photon and electron interactions in the energy interval 10 keV–100 MeV. Consequently, the substitutes are suitable for use in both dosimetric and image quality studies in diagnostic radiology, radiotherapy and radiation protection.

In the range of substitutes reported, the solid material making up the walls of the foam was designed to have a nominal mass density of 1000 kg m^{-3} (measured 1014 kg m^{-3}). A higher density, perhaps 1050 kg m^{-3}, could easily be achieved by decreasing the concentration of phenolic microspheres and increasing the CB2M concentration by an equal amount.

Although only five lung substitutes with mass densities ranging from 288 kg m^{-3} to 1014 kg m^{-3} are presented, any intermediate density may be produced by adjusting the DC1107 content. In applications where specific, precisely defined densities are required, a series of LN10 samples should be made, each with a different DC1107 concentration. The correct amount of DC1107 may then be interpolated from a plot of the mass densities of the hardened foamed samples versus DC1107 contents.

Certain grades of particulate filler, such as high purity magnesium oxide, have been found to cause the foam to collapse after an initial expansion. Similarly, concentrations of the foaming agent DC1107 in excess of 1% by mass can result in a partial collapse of the foam. Using the formulations and grades of fillers quoted in the previous section, no such problems should be encountered.

The sum of the elemental masses for lung given by ICRP (1975) is 97.7% of the quoted mass of the organ. Such a discrepancy will produce uncertainties in the calculated radiation interaction data, but the maximum errors in the ratios quoted in Table III from this source should be no more than 2%.

The LN10 series of substitutes may be used in the fabrication of both small (~ 100 cm^3) and large (~ 27 000 cm^3) lung phantoms. Pore size is, of course, more uniform in the smaller phantoms when large volumes of trapped air are more readily ejected from the bulk of the material. As the final product has a rigid structure, the material may be readily machined into blocks or sheets, although whenever possible, moulding directly into the desired shape and volume is preferable.

Acknowledgment

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REFERENCES

Alderson, S. W., Lanzl, L. H., Rollins, M. & Spira, J., 1962. An instrumented phantom system for analog computation of treatment plans. *American Journal of Roentgenology*, *87*, 185–195.

BERGER, M. J. & SELTZER, S. S., 1964. Tables of energy losses and ranges of electrons and positrons. *National Research Council Report 1133,* (National Academy of Science, Washington, D.C.).

CONSTANTINOU, C., 1978. Tissue substitutes for particulate radiations and their use in radiation dosimetry and radiotherapy. Ph.D Thesis, University of London.

EDLING, L., 1944. Experiences with rotation therapy. *Acta Radiologica, 15,* 427–443.

HUBBELL, J. H., 1969. Photon cross sections, attenuation coefficients and energy absorption coefficients from 10 keV to 100 GeV. *National Bureau of Standards, NSRDS—NBS 29.*

ICRP, 1975. *Report of the Task Group on Reference Man, ICRP Publication 23.*

ICRU, 1984a. *Stopping Powers for Electrons and Positrons, ICRU Report 37.*

——1984b. *Radiation Dosimetry. Electron Beams with Energies Between 1 and 50 MeV, ICRU Report 35.*

KIM, Y. S., 1973. Density effect in dE/dx of fast charged particles traversing various biological materials *Radiation Research, 56,* 21–27

MCGINLEY, P. H., 1973. Lung-equivalent material for fast neutron dose distribution studies. *International Journal of Applied Radiation and Isotopes, 24,* 477–478.

ROGERS, R. T., 1970. A phantom material to represent lungs. *British Journal of Radiology, 43,* 441–444.

STACEY, A. J., 1972 The absorption and scattering of radiation in heterogeneous media. M.Phil. Thesis, University of London.

STORM, E. & ISRAEL, H. I., 1970. Photon cross sections from 1 keV to 100 MeV for elements Z = 1 to 100. *Nuclear Data Tables, A7,* 565–681.

WHITE, D. R., 1974. The formulation of substitute materials with predetermined characteristics of radiation absorption and scattering Ph.D. Thesis, University of London.

——1977 The formulation of tissue substitute materials using basic interaction data. *Physics in Medicine and Biology, 22,* 889–899.

WHITE, D. R. & CONSTANTINOU, C., 1982. Anthropomorphic phantom materials. In *Progress in Medical Radiation Physics.* Ed by C. G. Orton (Plenum Press, New York), pp. 133–189.

WHITE, D. R., MARTIN, R J. & DARLISON, R., 1977. Epoxy resin based tissue substitutes. *British Journal of Radiology, 50,* 814–821.

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Case report

Thorotrast-associated mucoepidermoid carcinoma of the liver

By A. L. Lambrianides, B.Sc., F.R.C.S., A. R. Askew, Ch.M., F.R.C.S. and I. Lefevre, M.B., B.S.

Departments of Surgery and Histopathology, University of Queensland, Clinical Sciences Building, Royal Brisbane Hospital, Herston, Queensland 4036, Australia

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Thorotrast, once a popular radiographic contrast medium, is associated with an increased incidence of angiosarcoma, cholangiocarcinoma and hepatocellular carcinoma about 10 to 30 years after administration. Use of Thorotrast was discontinued in the 1950s primarily because of concern about potential long-term radiation effects.

CASE REPORT

A 59-year-old female had received prior Thorotrast administration for investigation of a right-sided cerebrovascular accident in 1952. She was admitted in 1984 for evaluation of right upper quadrant pain, anorexia, weight loss and jaundice. A plain radiograph of the abdomen showed irregular opacification of the liver parenchyma, dense opacification in the region of the spleen and opacification of the mesenteric lymph nodes.

Computed tomography (Fig. 1) showed a large tumour of the liver. A radionuclide liver scan confirmed the large mass in the liver, but an ultrasound examination was unhelpful. An arteriogram showed that the mass was hypovascular and a percutaneous needle biopsy demonstrated tissue consistent with squamous-cell carcinoma. The tumour was considered to be irresectable and her clinical condition rapidly deteriorated. She died 2 weeks after admission.

Pathological findings

At autopsy the liver was enlarged, weighing 2600 g. Occupying most of the right lobe was a tumour measuring 18 cm in greatest dimension. The cut surface of this tumour was a creamy-white colour with numerous areas of haemorrhage and necrosis, and surrounding this were peripheral nodules of tumour which merged into the main tumour mass. Tumour had invaded in a contiguous fashion into the superior pole of the right kidney but no evidence of tumour was found in any other location. The remainder of the autopsy findings consisted of a shrunken, hyalinised, calcified spleen weighing 17 g and similar dense fibrotic changes in abdominal lymph nodes and around the right carotid angiogram injection site. An extensive old cystic infarct was evident in the right cerebral hemisphere, associated with contralateral pyramidal tract atrophy.

Histology of the liver tumour showed it to consist predominantly of sheets and cords of squamous cells with occasional intercellular bridges and areas of keratin production (Fig. 2). Vascular invasion was evident, as was considerable sinusoidal dilatation of the liver at the edge of the tumour.

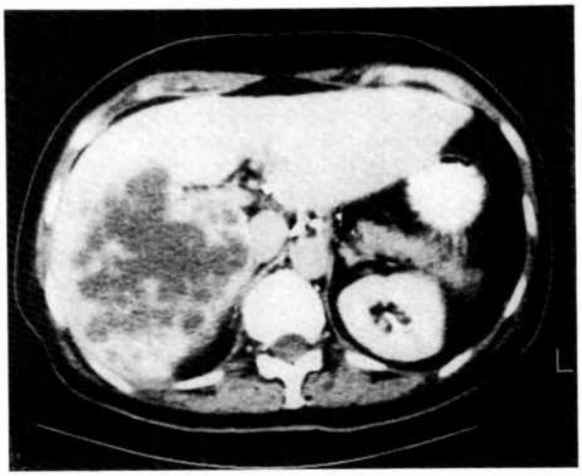

FIG. 1.

Computed tomogram demonstrating a large tumour mass within the liver substance.

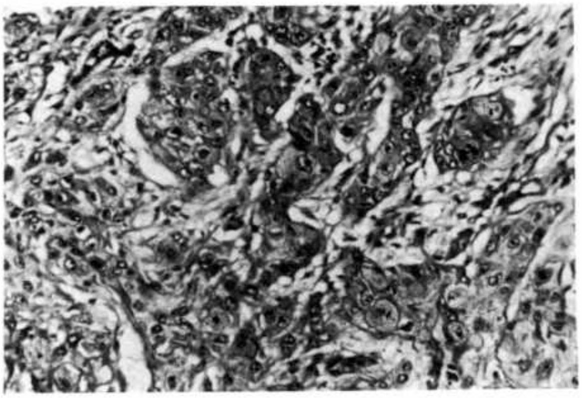

FIG. 2.

Primary mucoepidermoid carcinoma of the liver (haematoxylin and eosin, × 125).

Although no definite gland structures were seen, periodic acid-Schiff and mucicarmine stains for mucin were positive in the cytoplasm of some tumour cells. The non-neoplastic liver showed large accumulations of coarsely granular, brown, refractile pigment in portal tracts which represented Thorotrast.

Correspondence to: Dr A. L. Lambrianides, Department of Surgery.

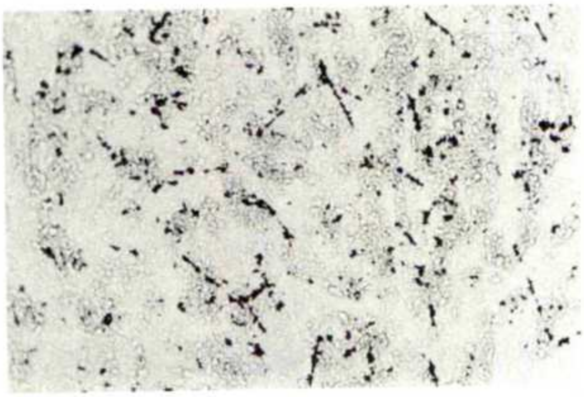

FIG. 3.

Autoradiograph showing alpha-particle tracks radiating out from deposits of thorium in the spleen.

The histology of the spleen, lymph nodes, vertebral bone marrow and carotid angiogram injection site showed dense, hyalinised fibrosis associated with Thorotrast deposition.

Transmission electron microscopy performed on the liver tumour showed the presence of desmosomes and tonofilaments and scanning electron microscopy and energy dispersive X-ray analysis of the brown granules confirmed them to consist of thorium. Autoradiography performed on the spleen confirmed the radioactive nature of the granules (Fig. 3).

In summary, the histological diagnosis was of a primary mucoepidermoid carcinoma of the liver associated with previous Thorotrast exposure, with Thorotrast deposition evident in the liver, spleen, abdominal lymph nodes, vertebral bone marrow and right carotid angiogram injection site.

DISCUSSION

Thorotrast is a colloidal solution which contains 20% thorium dioxide by weight. Its primary carcinogenic potential arises from the alpha particles which account for 90% of its radioactivity (Baserga et al, 1960; Da Silva Horta et al, 1965; Da Silva Horta, 1967; Janower et al, 1972; Gondos 1973). Following intravenous injection it is taken up by the reticulo-endothelial system, particularly by the liver and spleen, and most of it remains there indefinitely. Thorium has a physical half-life of 1.39×10^{10} years, while its 10 radioactive daughter elements have half-lives ranging from 6.7 years (^{228}Ra) down to 3×10^{-10} s (^{212}Po); alpha and beta particles and gamma rays are all produced at some stage in the disintegration. The tissues in which thorium is stored are, therefore, bombarded with ionising radiation for the rest of the patient's life. Thorotrast was widely used for angiographic procedures from 1930. Its use was discontinued in the 1950s primarily because of severe fibrotic reactions at the sites of extravasation and the concern about potential long-term radiation effects. Since the first report of Thorotrast-induced hepatic angiosarcoma appeared in 1947 (Macmahon et al, 1947) several epidemiological studies have demonstrated the association of hepatocellular carcinoma, cholangiocarcinoma and angiosarcoma with intravascular injections of Thorotrast (Faber, 1967; Hiraoka et al, 1981; Kojiro et al, 1982).

A total of 382 malignant hepatic tumours have been reported in patients who had received Thorotrast, with a mean latent period of 29 years (Scully et al, 1981). Thorotrast-induced mucoepidermoid carcinoma of the liver has not been reported previously. A careful search at autopsy in this case failed to reveal any tumour tissue outside the liver and, therefore, a diagnosis of primary hepatic carcinoma was thought to be reasonable, particularly in view of the long exposure of the liver to ionising radiation. The gross appearance of the tumour was a further factor in favour of its being a hepatic primary. As a rule, secondary deposits are multiple and are distributed throughout the liver; when solitary, they are usually small. This was a large tumour, confined to part of the right lobe. Multiple sections of the tumour demonstrated the presence of Thorotrast deposits within the tumour, and the presence of radiation was confirmed by autoradiography.

The association of Thorotrast and mucoepidermoid carcinoma of the liver in this patient may be coincidental, but the possibility of Thorotrast being the causative agent cannot be denied.

REFERENCES

BASERGA, R., YOKOO, H. & HENEGAR, G. C., 1960. Thorotrast induced cancer in man. *Cancer, 13*, 1021–1031.

DA SILVA HORTA, J., 1967. Late effects of thorotrast on liver and spleen, and their efferent lymph nodes. *Annals of the New York Academy of Science, 145*, 676–699.

DA SILVA HORTA, J., DA MOTTA, L. C., ABBATT, J. D. & ROTIZ, M. L., 1965. Malignancy and other late effects following administration of thorotrast. *Lancet, ii*, 201–205.

FABER, M., 1967. Thorium dioxide patients in Denmark. *Annals of the New York Academy of Science, 145*, 843–848.

GONDOS, B., 1973. Late clinical roentgen observations following thorotrast administration. *Clinical Radiology, 24*, 195–203.

HIRAOKA, T., KAMBARA, T., MORINAGA, T. & NAKAGAWN, S., 1981. Hemangioendothelial sarcoma of the liver after thorotrast injection. *Acta Pathologica Japonica, 31*, 813–861.

JANOWER, M. I., MIETTINEN, O. S. & FLYNN, M. J., 1972. Effects of long term thorotrast exposure. *Radiology, 103*, 13–20.

KOJIRO, M., KAWANO, Y., KAWASAKI, H., NAKASHIM, T. & IKEZAKI, H., 1982. Thorotrast induced hepatic angiosarcoma and combined hepatocellular and cholangiosarcoma in a single patient. *Cancer, 49*, 2161–2164.

MACMAHON, H. E., MURPHY, A. S. & BATES, M. I., 1947. Endothelial cell sarcoma of liver following thorotrast injection. *American Journal of Pathology, 23*, 585–611.

SCULLY, R. E., GALDABINI, J. J., MCNEELY, B. U., 1981. Case records of the Massachusetts General Hospital. *New England Journal of Medicine, 304*, 893–899.

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Case of the month

The man who hated hospitals

By D. J. W. Morewood and G. H. R. Lamb

Department of Radiology, Royal Liverpool Hospital, Liverpool

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A 40-year-old man who was otherwise well was seen in the outpatients department with an intermittent dull ache in the right upper quadrant of his abdomen, which had been present for 1–2 months. On examination, a mass was found at the site of the pain. Sonography (using a 3.5 MHz transducer) was performed and a transverse sonogram at the site of the mass is shown (Fig. 1). Further radiological investigation was recommended, but the patient failed to return to hospital. Two years later he returned with the same symptoms and the abdominal mass was by then larger. He was still otherwise well. His haemoglobin was 14 g/dl, white-cell count 660/mm^3 and his ESR 27 mm/h. Sonography was again performed and a longitudinal scan from this examination is shown (Fig. 2). Computed tomography (CT) was then carried out (Fig. 3).

From where is the mass arising and what is your differential diagnosis?

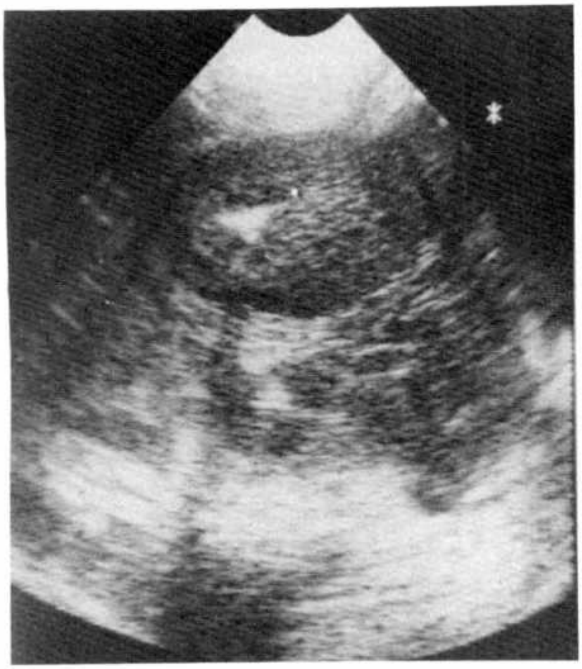

FIG. 1.

Initial transverse sonogram over the mass.

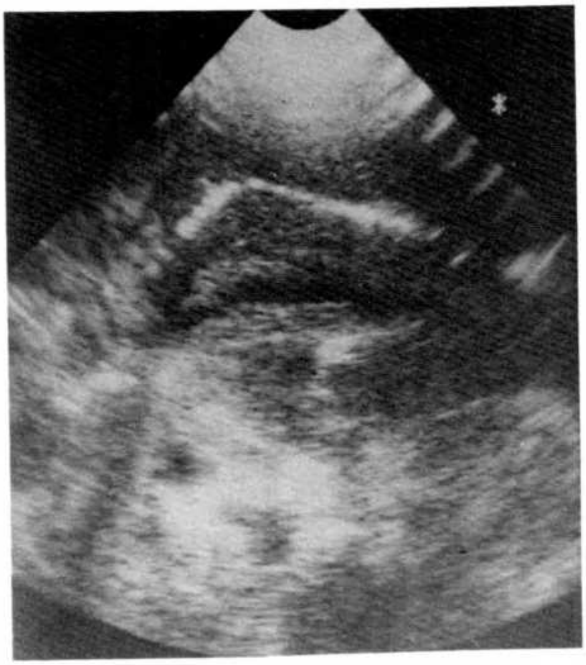

FIG. 2.

Longitudinal sonogram obtained at the patient's attendance 2 years later. The transverse scan was little changed.

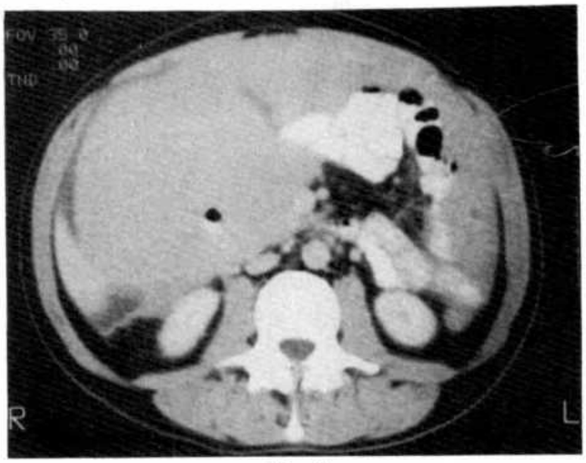

FIG. 3.

Computed tomography section through the abdominal mass.

The typical "bull's eye" or "target" appearance produced on the transverse sonogram by an eccentric triangular echogenic centre within a surrounding irregular echolucent area is a sign of gas within a surrounding soft-tissue mass. The site suggests that it may be a colonic lesion. The longitudinal scan shows a long echogenic centre with surrounding echolucency. These appearances are confirmed by the CT section (Fig. 3), which shows a large mass surrounding a narrow, gas-containing lumen.

The differential diagnosis at this stage in a patient who had been relatively well for 2 years was between colonic lymphoma and a benign tumour, such as a leiomyoma. A barium enema was performed next and showed a stricture in the right side of the colon beyond which no barium passed. Some rapid-transit barium was given orally and a radiograph made 1 h later (Fig. 4) shows the extent of the constricting soft-tissue mass. The next step was to obtain tissue for diagnosis and a Trucut biopsy was performed under local anaesthetic with fluoroscopy. The histology showed a diffuse centroblastic, centrocytic lymphoma (a low grade non-Hodgkin's lymphoma). The patient was then treated with chemotherapy.

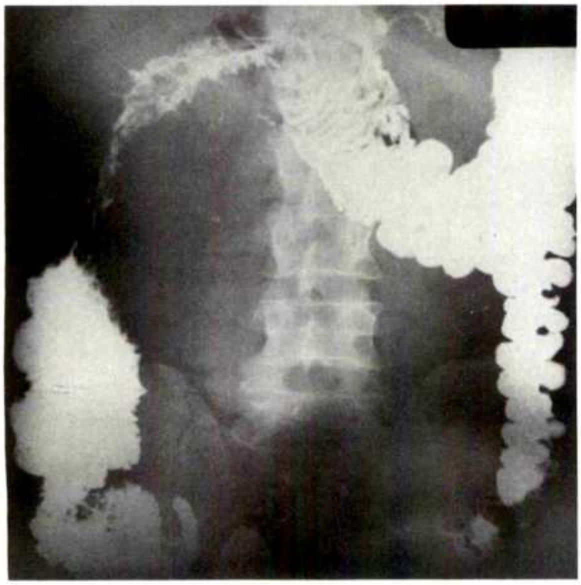

FIG. 4.

Radiograph after combined barium enema and oral barium.

DISCUSSION

The most common symptom in colonic lymphoma is abdominal pain over the site of the tumour, a palpable mass occurring in over 60% (Zornoza & Dodd, 1980). Lymphoma of the gastrointestinal tract is thought to be a B-cell tumour and has a tendency to remain localised to the gut wall with subsequent spread to draining lymph nodes (Brady & Asbell, 1980). The caecum is the most common site for primary colonic lymphoma (O'Connell & Thompson, 1978).

Any condition producing bowel-wall thickening, such as carcinoma, lymphoma, benign intestinal tumour or Crohn's disease, may be demonstrated by sonography and will cause a "target" or "bull's eye" lesion (Fleischer et al, 1980). However, on CT, lymphoma showed the greatest thickening of the bowel wall (Megibow et al, 1983).

Colonic lymphoma produces a spectrum of appearances on barium enema related to whether the lymphoma originates in the bowel or involves it secondarily. This case of primary lymphoma presented as a large mass, which is the most characteristic finding (O'Connell & Thompson, 1978), and the most effective way of making a definite diagnosis is to obtain tissue for histology when the mass has been localised.

REFERENCES

BRADY, L. W. & ASBELL, S. O., 1980. Malignant lymphoma of the gastrointestinal tract. *Radiology*, *137*, 291–298.

FLEISCHER, A. C., MUHLETALER, C. A. & EVERETTE JAMES, A., 1980. Sonographic patterns arising from normal and abnormal bowel. *Radiologic Clinics of North America*, *18*, 145–159.

MEGIBOW, A. J., BALTHAZAR, E. J., NAIDICH, D. P. & BOSNIAK, M. A., 1983. Computed tomography of gastrointestinal lymphoma. *American Journal of Roentgenology*, *141*, 541–547.

O'CONNELL, D. J. & THOMPSON, A. J., 1978. Lymphoma of the colon: the spectrum of radiologic changes. *Gastrointestinal Radiology*, *2*, 377–385.

ZORNOZA, J. & DODD, G. D., 1980. Lymphoma of the gastrointestinal tract. *Seminars in Roentgenology*, *15*, 272–287.

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Short communication

The synergism between hyperthermia and ionising radiation

By J. A. G. Holt, F.R.C.S., F.R.C.R., F.R.A.C.R. and R. W. Stanford, M.A., C.Phys., F.R.A.C.R.(Hon.)

The Radiotherapy Centre, 24 Salvado Road, Wembley 6014, Western Australia

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The experimental survival curve for irradiated cells can be represented by

$$N/N_0 = 1-(1-e^{-D/D_0})^n$$

where there are N survivors from an initial population of N_0 after dose D, D_0 is the dose required for one "hit" per target and n targets are irradiated (Johns, 1964). When clinically derived values of D_0 and n are used in this equation the resulting curve fits experimental results (Andrews, 1968). Factors affecting D_0 and/or n change the ratio N/N_0 for a given dose D. Hyperbaric oxygen is one such factor (Deschmer & Gray, 1959; Gray, 1961) and a rise in the temperature of the irradiated cells another (Dewey & Freeman, 1980). The change produced by this latter effect is in a favourable direction (Westra, 1971). For this change to be clinically valid, hyperthermia in conjunction with ionising radiation must neither be toxic to normal tissue nor increase the morbidity of the X-ray dose on normal tissue. At 41.8°C, the limiting temperature for human liver, there is no demonstrable harm to normal tissue (Law & Pettigrew, 1980) nor is the radiation effect on the normal potentiated (Overgaard & Nielson, 1980; van der Zee et al, 1985).

Electromagnetic non-ionising radiation (EMR) offers an easy means of raising the temperature of the cancer and the host while delivering X-ray therapy and has been extensively investigated *in vitro* and *in vivo* (Joines et al, 1980). Moreover, the relevant electrical characteristics of the cancer give rise to greater absorption of the radiation in the cancer than in normal tissue. Thus the cancer is selectively heated and normal tissue remains relatively cool.

Thus, EMR-induced hyperthermia has the potential to "shield" normal tissue while maintaining its increased cell kill ratio, N/N_0 per unit of X-ray dose applied. That this ratio for EMR is greater than for the identical temperature created by non-EMR methods has been demonstrated (Joines, 1977). All frequencies of EMR have a beneficial effect. Until the alterations in the values of D_0 and n that they create can be measured, the optimum frequency can only be established by clinical trials. These will also demonstrate the optimum doses and temporal relationships of X-rays and EMR.

As with wax bath or simple hyperthermia, the toxic effects of EMR alone and in combination with X-ray therapy must be tolerable and not potentiate normal tissue sequelae and morbidity. The lack of toxic effects of EMR in isolation is amply demonstrated by 50 or more years use of 13, 27, 434, 918, 2500 MHz and other frequencies in physiotherapy practice. Many thousand items of EMR-generating equipment irradiate millions of people daily, without any reported ill effects (Schwan, 1965). When combined with X-ray therapy there is no published categoric evidence which indicates that X-irradiation sequelae are deleteriously enhanced by the additional use of EMR. On the contrary, it has been shown (Perez et al, 1983; Law et al, 1985) that the combined method may be used with safety to treat again areas already previously treated to accepted full conventional levels (Scott et al, 1984).

In 1973 and 1974, whole-body simple hyperthermia (41.8°C for 6 h immersion in a hot wax bath), although creating a small increase in radiosensitivity, proved to be cumbersome and tedious. It was replaced by EMR-induced heating. In March 1974, 12 Erbe UHF 69, 434 MHz 200 W physiotherapy heating units replaced the wax bath. This equipment has been described and illustrated by Holt (1975, 1980).

Head and neck cancer was chosen for the pilot study. All such patients presenting consecutively to this unit between March 1974 and May 1975 were treated using a combination of EMR and ionising radiations. Twice weekly (Mondays and Wednesdays) the cancer areas were irradiated with EMR by positioning the patients so that their cancers were in the approximate centre of the machine (Holt, 1980, Fig. 2A). Ten minutes of EMR treatment, 20 min of rest, 15 min of EMR treatment was followed as soon as possible by 200 cGy uniformly delivered to the tumour volume by megavoltage irradiation. On the three other weekdays, 200 cGy only was given. In this series the average dose given was 4600 cGy in 8 weeks (range 1500–6000 cGy).

TABLE I

AN ANALYSIS OF 401 PATIENTS WITH HISTOLOGICALLY PROVEN PRIMARY HEAD AND NECK CANCER (92% SQUAMOUS CELL CARCINOMA) TREATED BY SEQUENTIAL EMR AND IONISING RADIATION (EMR COLUMNS) AND IONISING RADIATION ALONE (SVT COLUMNS)

	1978 report		1985 report	
	EMR	SVT	EMR	SVT
Total patient No. in each group	52	52	79	218
Average age (years)	71	69	63	68
Site of primary (%)				
Larynx	13.5	13.5	28	26
Pharynx, pyriform fossa	23	32	14	13
Mouth, tongue, tonsil, palate	48	40	25	36
Nose, nasopharynx, sinuses, ear	13.5	11.5	19	12
Salivary glands	2	4	14	12
Staging				
T_3 and T_4	50	50	31	57
N_2 and N_3	40	45	38	49
Complete primary resolution (%)	94	36	92	34
Crude 3-year survival (%)	54	19	68	17
Crude 8-year survival (%)	40	11	NA	NA

NA = not applicable.

After 14 months 52 patients had been treated. They were compared with 52 similar cancers treated consecutively to the same date on a 4 MeV accelerator (SVT). average 6000 cGy, range 4800–6600 cGy, and with 52 similar cancers treated under 303 kPa oxygen tension (HPO)· 5–7 fractions, 3000–3850 cGy consecutively up to May 1975 These three groups were followed for 3 years for the first report (Nelson & Holt, 1978). The striking improvement in complete primary resolution (94% EMR, 62% HPO, 36% SVT) and 3-year crude survival (60% EMR, 23% HPO, 19% SVT) encouraged continuation of the combined therapy. A further 79 patients were treated until May 1982 for a crude 3-year survival of 68%, while conventional therapy treated 218 patients for a 17% crude survival rate (Holt & Nelson, 1985). Brief details are given in Table I.

In conclusion, therefore, the regime which must kill more cancer cells per cGy and, thus, must improve the current results of X-ray therapy has to be some combination of EMR and ionising radiation.

REFERENCES

ANDREWS, J. R., 1968. *The Radiobiology of Human Cancer Radiotherapy* (W. B. Saunders Co., Philadelphia), pp. 11–15, 48–106.

DESCHNER, E E. & GRAY, L. H., 1959. Influence of oxygen tension in x-ray induced chromosomal damage in Ehrlich ascites tumour cells irradiated *in vitro* and *in vivo*. *Radiation Research*, *11*, 115–122.

DEWEY, W C. & FREEMAN, M L., 1980. Rationale for use of hyperthermia in cancer therapy. *Annals of the New York Academy of Sciences*, *9*, 372–378.

GRAY, L H., 1961. Radiobiologic basis of oxygen as a modifying factor in radiation therapy. *American Journal of Roentgenology*, *85*, 803–819

HOLT, J. A. G , 1975. The use of VHF radiowaves in cancer therapy. *Australasian Radiology*, *19*, 223–241.

——1980. Alternative therapy for recurrent Hodgkin's disease—radiotherapy combined with hyperthermia by electromagnetic radiation to create complete remission in 11 patients without morbidity. *British Journal of Radiology*, *53*, 1061–1067

HOLT, J A G. & NELSON, A. J. M., 1985 Combined microwave therapy. *Medical Journal of Australia*, *13*, 707–708.

JOHNS, H E., 1964 *The Physics of Radiology* 2nd edit. (Charles C. Thomas, Illinois), pp. 660–668.

JOINES, W. T., 1977. Optimizing the heat treatment of tumors by microwaves. In *Clinical Prospects for Hypoxic Cell Sensitisers and Hyperthermia*. (University of Wisconsin), pp. 228–237.

JOINES, W. T., JIRTLE, R. L., RAFAL, M. D. & SCHAEFER, D. J., 1980. Microwave power absorption differences between normal and malignant tissue *International Journal of Radiation Oncology Biology Physics*, *6*, 681–687.

LAW, H. T. & PETTIGREW, R. T., 1980. Heat transfer in whole body hyperthermia. *Annals of the New York Academy of Sciences*, *9*, 298–308.

LAW, M. P , AHIER, R. G & SOMAIAS, 1985. Thermal enhancement of radiation damage in previously irradiated skin *British Journal of Radiology*, *58*, 161–167

NELSON, A. J. M & HOLT, J A. G., 1978. Combined microwave therapy. *Medical Journal of Australia*, *2*, 88–90.

OVERGAARD, J. & NIELSEN, O S , 1980. The role of tissue environmental factors on the kinetics and morphology of tumour cells exposed to hyperthermia. *Annals of the New York Academy of Sciences*, *9*, 254–278.

PEREZ, C A., EMAMI, B. N., NUSSBAUM, G. H., VAN GERICHTEN, D., LEYBOVICH, L. & SMITH, L., 1983 Clinical results with irradiation and local microwave hyperthermia in cancer therapy. Proceedings of 25th Annual Meeting ASTR. *International Journal of Radiation Oncology Biology Physics*, *9*, Supp. i, pp. 83–84.

SCHWAN, H. P., 1965. The biophysics of diathermy In *Therapeutic Heat and Cold*. Ed. by S. Licht (New Haven, Connecticut), pp 63–123.

SCOTT, R. S , JOHNSON, R. J. R , STORY, K. V. & CLAY, L , 1984. Local hyperthermia in combination with definitive radiotherapy increased tumour clearance, reduced recurrence rate in extended follow-up. *International Journal of Radiation Oncology Biology Physics*, *10*, 2119–2123.

WESTRA, A., 1971. The influence of radiation on the capacity of *in vitro* cultured mammalian cells to proliferate. Academic Thesis, translated by B Dewey (Colorado State University).

ZEE, VAN DER, J , VAN RHOON, G C & WIKE-HOOLEY, J L , 1985. Clinically derived dose effect relationship for hyperthermia given in combination with low dose radiotherapy. *British Journal of Radiology*, *58*, 243–250.

1986, *The British Journal of Radiology*, 59, 797–798 AUGUST 1986

Correspondence

(The Editors do not hold themselves responsible for opinions expressed by correspondents)

Calibration of rectal dose-rate monitors

THE EDITOR—SIR,

In common with many radiotherapy departments, it is standard practice at the Glasgow Institute of Radiotherapeutics and Oncology to measure the dose-rate to the recto-vaginal septum following a gynaecological caesium insertion. This checks that the treatment applicators and vaginal packing are suitably positioned to reduce the dose received by the recto-vaginal septum to clinically tolerable levels.

Experience has been gained of two types of rectal dose-rate monitors, namely the Therados DRM-1 and the Vertec VS102. Three of each type were purchased for use in the hospitals served by the Institute. The purpose of this communication is to forewarn users of a potential calibration error which will arise with the DRM-1 if the calibration source has a different radiation quality from the sources used in the treatment applicators.

Until 1980, conventional Manchester applicators were used and rectal dose-rates of typically 20–80 cGy h^{-1} were measured in theatre using the DRM-1 monitor. Since then most of the treatments have been carried out using a low dose-rate Selectron afterloading unit. In order to preserve the radiation protection advantages of this technique the rectal dose is assessed using low activity caesium test sources positioned manually in the applicators during theatre (Corner et al, 1982). The DRM-1 monitors were found to be unsuitable for measuring these low dose-rates (2–8 cGy h^{-1}) and were superseded by the more sensitive and stable Vertec VS102 monitor. Whilst commissioning the latter, inconsistencies between the DRM-1 and VS102 monitor were noted. Subsequent investigations showed the main reason to be a very marked difference in the energy response of the detectors to the radiation qualities being measured.

Energy dependence

The DRM-1 detector is an n-type silicon junction diode encapsulated near the tip of a brass tube (5 mm o.d. and 3 mm i.d.). The data supplied by Therados on its energy dependence is reproduced in Table I. The VS102 detector is a lithium drifted p-type silicon diode mounted near the tip of a stainless steel tube (6 mm o.d.) and the manufacturers claim its relative response is unity for energies above 250 keV, rising at energies below 250 keV to a maximum of approximately 1.6 in the region of 80 keV.

TABLE I

REPRODUCED FROM THERADOS TECHNICAL SPECIFICATION

Quality		Response (rad nC^{-1})
kV	Filter	
100	1 Al	1.95
140	4 Al	0.96
170	0.5 Cu	0.66
200	0.5 Cu	0.63
220	Sn	0.55
^{60}Co		0.60

The response of the detectors was compared in three calibration fields of different quality ^{60}Co and ^{137}Cs γ rays and an orthovoltage radiotherapy beam (300 kV, 12 mA, filtration = 2.5 mm Cu, HVL = 2.5 mm Cu).

Cobalt-60 versus caesium-137 radiation

The dose-rate monitors were calibrated at the Scottish Centre of the National Radiological Protection Board (NRPB), on the facility used to calibrate personnel survey meters. In normal use the rectal probes are fitted with a perspex sheath to increase their diameter to 10 mm in order to reduce the likelihood of perforating the rectal wall. Having confirmed that these perspex sheaths provided adequate build-up for accurate in-air measurements in a ^{60}Co γ-ray field, the detectors were placed at fixed distances from calibrated ^{60}Co and ^{137}Cs radiation sources. The source exposure rates at 1 m had been accurately determined by Amersham International plc. A perspex sheet was placed between the source and detector to eliminate any electron contamination in the field. The exposure rates from the sources were such that readings could be taken on the same scale range. When the ratios of the measured dose-rates from the two sources were compared with the expected ratio, the sensitivity of the Vertec was confirmed to be uniform with ±3% whereas the Therados detectors were 23% less sensitive to the ^{60}Co radiation.

Orthovoltage versus caesium-137 radiation

The dose-rate monitors were calibrated using a Siemens Stabilipan orthovoltage unit. The probes were placed at 5 cm depth in a perspex phantom positioned as far as possible from the tube focus, the dose-rate was 142 cGy h^{-1}.

Measurements were then taken in the Institute's caesium-137 calibration pot. The dose-rate in this pot had previously been determined as 6.6 cGy h^{-1}, verified by computer calculations and by comparative measurements against the Selectron treatment sources. The dose-rate monitor readings required different settings of the scale range switch and corrections were applied for non-linearity between ranges.

The Therados detector was found to be 32% less sensitive to orthovoltage radiation in direct contrast to the Vertec detector, which was 89% more sensitive.

Discussion

The results for the energy dependence of the VS102 detector show that its relative response is unity for ^{60}Co and ^{137}Cs radiation, rising to 1.89 at the orthovoltage beam quality used in the above experiment. In the case of the Therados detector, if its response to ^{60}Co γ rays is taken as unity, the relative responses to ^{137}Cs and the orthovoltage beam are 1.3 and 0.88, respectively.

The Therados user manual suggests that the dose-rate monitor can be calibrated by "placing the probe in a radiation field with a well known dose-rate (*e.g.* in a solid phantom in a ^{60}Co field). . .". However, if the user then assumes that the detector response is reasonably flat from 220 kV to the energy of ^{60}Co γ rays, Table I giving response factors varying between

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0.55 and 0.60 rad nC^{-1}, a significant dosimetry error will occur unless the treatment sources are to be ^{60}Co. Since our results show that the detector's response to ^{137}Cs γ rays is about 30% greater than for ^{60}Co γ rays, measurements taken in patients treated with ^{137}Cs will be overestimated. A similar error will occur if orthovoltage radiation is used.

The energy response of semiconductor radiation detectors can vary from one detector to another of the same type and may also be dependent on age, dose, dose-rate and temperature. We would recommend that every time such detectors are used they are calibrated in a calibration pot containing the same radionuclide as that to be used for treatment. This pot should be calibrated against the treatment sources.

The Vertec and Therados probes are temperature sensitive, each having a temperature coefficient of typically 0.05 cGy h^{-1} per °C over the temperature range 22–37°C. The perspex sheaths fitted to our probes insulate the detectors and reduce the rate of temperature rise. This permits measurements of rectal dose-rate to be taken with instruments calibrated at room temperature.

The authors would like to thank the NRPB Scottish Centre for the use of its calibration facilities and Mr D Orr for his assistance with the measurements.

Yours, etc ,
R. Thomas
R C. Lawson

West of Scotland Health Boards,
Department of Clinical Physics & Bio-Engineering,
11 West Graham Street,
Glasgow G4 9LF

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REFERENCE

Corner, G A., Skinner, D. L & Watson, E R., 1982. Selectron: rectal dose-rate measurements and modified applicators. *Clinical Radiology, 33*, 477–480.

Assessment of priorities when introducing some radiation protection methods in radiodiagnosis

The Editor–Sir,

I write to endorse wholeheartedly the points regarding the benefits of rare-earth imaging systems made by Russell (1986) Obviously one of the ways of reducing radiation dose to the patient is to reduce the amount of X-ray energy required to produce a diagnostic film. The use of a high speed rare-earth system not only enables low patient dose to be achieved, but in many cases improves image quality.

It was found very early on in the development of rare-earth phosphor materials that their high X-ray absorption and conversion efficiencies could enable large exposure reductions to be achieved and still produce the same light output as that of a calcium tungstate system. This increased efficiency meant significant real cost savings could be achieved and, more importantly, measured, as indicated below.

As lower doses are required and in particular lower mA s settings, the reduction has the effect of considerably extending the life of the X-ray tube (as life is proportional to thermal load) Capital costs can be reduced on the purchase of new equipment as lower-powered generators can be purchased. Likewise, the level of electrical energy used in equipment is a determining factor in the incidence of breakdowns and electrical faults, thus the use of lower input/output energies can offer savings in maintenance and energy costs.

However, system speed in terms of single exposure reduction should not be the only consideration. The use of a low mA will effectively reduce the "blooming" of the X-ray tube filament, thereby reducing the effective focal-spot size. Likewise, a reduction in current load will allow a greater access to the fine focus and in turn reduce the effect of geometric unsharpness on the final radiograph. Since short exposure times can be used, the chance of movement unsharpness is reduced thereby reducing the need to repeat radiographs

The increased resolution capabilities of rare-earth phosphors may in turn allow a greater level of initial diagnosis without the need to request further views, thus reducing further the radiation dose to the patient.

Many recent advances have been made in commercially available rare-earth systems. Lately, there has been a great deal of activity in optimising the sensitivity of orthochromatic (green) sensitive film. Modified film grain has been used to increase resolution and the development of anti-crossover coating techniques has extended the resolution capabilities of current film. Similarly, screen optimisation, *i.e.* better output of light at a specific wavelength, has been developed in the area of green-emitting systems to provide maximum screen efficiency.

In conclusion, it is evident that the age of rare-earth imaging is upon us. The time is right to take a look at the imaging techniques employed in radiology departments and to match them against the exposure levels required to produce those images.

Yours, etc.,
D. G Rothery

3M United Kingdom plc,
3M House,
PO Box 1,
Bracknell,
Berkshire RG12 1JU

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REFERENCE

Russell, J G. B., 1986 Assessment of priorities when introducing some radiation protection methods in radiodiagnosis. *British Journal of Radiology, 59*, 153–156.

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Radiology '86: forty-fourth Annual Congress and Scientific Exhibition, held in Bristol, April 9–11, 1986

Opening Session: Mackenzie Davidson Memorial Lecture

ADVANCES IN TECHNOLOGY AND THEIR IMPACT ON MEDICINE

A. R. Margulis and W. J. Shea Jr

Department of Radiology, University of California, San Franciso, California, USA

The tremendous advances in imaging technology are occurring at a time when expenses for health are exceeding the willingness of governments to permit further increases. In the US the 1984 expenditures of 387.4 billion dollars represented close to 11% of the gross national product, while in 1965 it amounted to only 6.1% of the GNP. Regulating the availability of the new imaging modalities was a failure in the US as CT particularly proved to be cost effective. Ultrasound, CT and especially interventional radiology have shown to be not only cost effective but have been beneficial to patients because of reduction in invasiveness. Magnetic resonance imaging promises further dramatic advances in the same direction.

The development of algorithms for the proper sequential use of the various imaging modalities is imperative but needs to be governed entirely by local and temporal considerations. The largest health expenditures are technology related but are based on ethical considerations: how many technological advances should be used to prolong life for the critically ill, the newborn or the elderly?

Managing Radiology

Chairman: Dr J. Roylance
Introduction: Dr J. Roylance

Performance indicators in radiology, by Dr P. Bourdillon
Maximising cost effectiveness in diagnostic departments, by Dr P. Davies
Maximising cost effectiveness of cancer treatment, by Dr F. E. Neal
Quality improvement techniques, by Mrs J. Harvey
Planning for changing needs, by Dr R. J. Maxwell

PERFORMANCE INDICATORS IN RADIOLOGY

P. J. Bourdillon

DHSS, London

A revised package of performance indicators was issued to the NHS in 1985 to help clinicians and others responsible for managing resources to assess aspects of performance which need further investigation and action. There are currently three performance indicators covering radiology aimed at providing an assessment of cost and manpower efficiency. The indicators are based on radiographic work units (RWUs). They show respectively revenue expenditure, consultant radiologist whole-time equivalents (WTEs) and radiographer WTEs in relation to RWUs. With the introduction of Korner it is proposed that the RWUs be phased out. The Korner Working Group divided radiological procedures into six categories. Potentially this could generate an unwieldy 18 (6 × 3) performance indicators in radiology. Thus, for the purposes of departmental analysis and the development of more robust performance indicators in radiology, it is felt important to develop a quantitative relationship between the six categories to provide acceptable weightings.

Some financial information about radiology departments is now available from Corbett Hospital, Guy's Hospital, Coventry and Warwickshire Hospital and Walsgrave Hospital. It has been shown that the sum of the costs of the consumables and the salaries at Guy's Hospital for a particular procedure can be used as a representative index for the revenue costs of that investigation at each of the other three hospitals. Data is available for this sum on 105 of the 131 radiological procedures listed in the Korner Schedule. On the basis of this index, six radiological procedures, including CT, have been identified as probably being inappropriately classified in the Korner Schedule. Reallocation of these six procedures suggests the following quantitative relationship between Korner Groups A–F: 1; 2.5; 6; 12; 30; 60.

MAXIMISING COST EFFECTIVENESS IN DIAGNOSTIC DEPARTMENTS

P. Davies

City Hospital, Nottingham

Patients are referred for help in solving clinical problems. The first task is to eliminate those examinations that do not contribute to patient care. New techniques should only be introduced if they are diagnostically better than old ones. They should not be introduced if neither affordable nor effective. There are figures for comparison of the effectiveness of the departments and the relationship of numbers of rooms to staffing levels under standard average conditions of work. Performance indicators can be readily calculated, but the comparison of statistics is difficult because of workload mix. This is compensated for by using work units. The number of patient attendances and examinations needs to be known, as well as the standard units.

More than 80% of the budget of an X-ray department is committed because of its capacity. The remainder does not allow much scope for short-term savings. Efficiency can only be achieved by long-term strategies but can be quickly lost by ill-considered expenditure. An effective strategy for cost-effectiveness is:

to report all films as soon as possible;
to take decisions on the minimum number of examinations;
to eliminate unnecessary examinations by discussion with clinicians; and
to avoid pushing up costs by using unnecessarily expensive items.

MAXIMISING COST EFFECTIVENESS OF CANCER TREATMENT

F. E. Neal

Weston Park Hospital, Sheffield

It is accepted that effective management for cancer patients is expensive, partly due to the high capital cost of radiation therapy equipment and cytotoxic drugs, but also because of considerable revenue consequences that are involved. The provision of optimal clinical care is the most important consideration which must be carefully preserved and not eroded by the desire to save money, but the great variation in clinical practice from centre to centre complicates the issues and there are probably many different approaches to achieving cost effectiveness. At national, regional and unit level, the provision of optimum care is dependent on the effects of population size and trends, cancer incidence and the specific patient referral pattern in any given area. Although DHSS guidelines have been provided for the type and size of radiation equipment required per head of population, there are many other aspects of the problem which have to be considered. Some of these are

(i) geographical distribution of cancer treatment centres,
(ii) provision of modern and effective radiation therapy equipment and the introduction of realistic equipment replacement programmes;
(iii) the control of cyctotic drug therapy and the introduction of safe working practices,
(iv) methods of providing optimum radiographer staffing levels,
(v) possibility of using shift system to extend the "clinical" day;
(vi) geographical problems,
(vii) patient flow pattern through departments,
(viii) transport facilities,
(ix) inpatient accommodation—hostel accommodation;
(x) supporting services;
(xi) availability of diagnostic aids,
(xii) management of patients receiving cytotoxic therapy,
(xiii) after care services

Several of these aspects are critically examined to ascertain whether varying current practices could produce better care with reduction of revenue costs.

QUALITY IMPROVEMENT TECHNIQUES

M. J. Harvey

Middlesex Hospital, London

Quality assurance in diagnostic radiology has concentrated on the production of a quality image and in particular on the performance of the equipment used to produce the image. Other aspects of "quality" such as effectiveness, timeliness and customer satisfaction are rarely considered. Quality improvement techniques are used regularly in industry as a systematic method of assessing performance and identifying methods of improvement. Such techniques have had limited applications in the Health Service.

The superintendent radiographers from five London hospitals have formed a group with the aim of establishing project teams within each department. These teams will identify areas for improvement and, using techniques such as brain storming and cause and effect analysis, establish and implement remedies. The success of these projects will depend on the commitment of those involved, not only the project teams but also those people who have the authority to see that remedies are implemented. This is of particular importance when the remedies cross departmental boundaries. Each of the five superintendents will be seeking "sponsorship" within their own hospital to ensure this support. It is hoped to have the teams in each hospital active by the beginning of February 1986. Their progress to date and future intentions are presented.

PLANNING FOR CHANGING NEEDS

R. J. Maxwell

King Edward's Hospital for London

Angiography Update

Chairman: Dr W. D. Jeans

Recent developments in angiography, by Dr D. J. Allison

Percutaneous laser thermal angioplasty in complete arterial occlusions, by Dr D. C. Cumberland, Dr D. I. Tayler, Mr C. L. Welsh and Dr D. J. Moore

Renal angioplasty—a review of 40 cases, by Dr C. Evans and Dr M. Ruttley

Direct puncture embolisation with spring emboli, by Dr A. P. Hemingway and Dr D. J. Allison

Venous vs arterial DSA, by Professor H.-J. Maurer

A clinical study of intra-arterial subtraction angiography in severe peripheral vascular disease, by Dr D. McInerney, Dr K. Maher, Dr D. Bouchier-Hayes and Dr A. Walsh

The reproducibility of quantifying the degree of stenosis using digital fluorography, by Dr P. C. Jackson, Mr H. Key, Dr E. Thomas, Dr W. D. Jeans and Professor E. Rhys Davies

Comparative testing of Gruntzig balloon diameters and bursting pressures, by Dr J. H. L. Henson, Dr W. D. Jeans, F. J. Newham, C. Paice and A. Blakeborough

RECENT DEVELOPMENTS IN ANGIOGRAPHY

D. J. Allison

Department of Diagnostic Radiology, Hammersmith Hospital, London

Advances in non-invasive imaging technology such as ultrasound, CT, MRI and radionuclide scanning have resulted in the reduced application and in some cases the virtual disappearance of certain angiographic procedures. There are, however, five developments operating in the opposite direction and which seem certain to ensure that angiography will remain an important subspecialty for the foreseeable future.

(i) *New contrast media.* The new low osmolality media have made angiography safer and more comfortable for the patient, and developmental work continues to produce improvements in this area.
(ii) *Digital subtraction techniques.* Digital vascular imaging has had an enormous impact on angiographic practice

It enables us both to increase the range of possible examinations available to a patient and to perform those we elect to do more efficiently and safely.

(iii) *Technical advances.* Advances in the technology of catheters, wires, and other instruments continue to make angiography safer and easier to perform. The stimulus to many of these new developments has arisen from the requirements of the interventional radiologist.

(iv) *Interventional radiology.* Interventional vascular procedures grow steadily in their application and scope, and new techniques in this area are being constantly generated as a result of the close liaison that has been created between interventional radiologists and equipment manufacturers.

(v) *Angioscopy.* One of the most recent developments in the field of vascular radiology has been the introduction of angioscopy. Though still in an experimental stage, it offers exciting possibilities for future diagnosis and therapy, particularly in view of concurrent advances in medical laser technology.

PERCUTANEOUS LASER THERMAL ANGIOPLASTY IN COMPLETE ARTERIAL OCCLUSIONS

D. C. Cumberland, D. I. Tayler, C. L. Welsh and D. J. Moore

Northern General Hospital, Sheffield

A major limitation of percutaneous angioplasty is the difficulty of crossing complete occlusions. Laser energy can vaporise thrombus and atheroma, but its potential will not be realised until an intra-luminal channel can be produced while reliably avoiding vessel-wall perforation. We have used a metal-tipped laser fibre (laser probe) with up to 10 W argon laser power for 5–60 s to traverse 28 complete occlusions of 1–35 cm length (mean 8 cm). Nineteen were initially probed at their proximal limits by a guide wire, to classify them as potentially "easy" or "difficult" to cross by conventional means. Nine occlusions were "impossible" either because previous angioplasty attempts had failed or because of anatomical unsuitability for conventional techniques. The probe successfully traversed all nine "easy", nine of 10 "difficult" and six of nine "impossible" occlusions. In all successfully traversed lesions an adequate initial channel (mean lumen diameter (MLD) 1.15 mm ± 0.4 (SD)) was produced for subsequent balloon dilatation (MLD 2.81 mm ± 0.91). In one case mechanical wall entry with extravasation occurred (before laser energy was used), probably due to a false passage produced by a prior guide wire; there were no sequelae.

Thus, the laser probe facilitates percutaneous recanalisation and can cross some occlusions impossible by conventional techniques. This has potential for increasing the role of angioplasty in arterial disease.

RENAL ANGIOPLASTY: A REVIEW OF 40 CASES

C. Evans and M. Ruttley

Department of Radiology, University Hospital of Wales and Cardiff Royal Infirmary

Renal angioplasty has been attempted in 40 patients with hypertension. No attempt was made in this study to assess the significance of the stenoses by peripheral or renal vein renins prior to angioplasty. The patients were divisible into those with unilateral fibromuscular dysplasia (FMD) (nine), bilateral FMD (one), unilateral atheroma (10), bilateral atheroma (15), and transplant artery stenosis (five). The best therapeutic response was in patients with unilateral FMD. Seven out of nine were normotensive between 6 months and 3 years after the procedure. In atheromatous stenosis, about two-thirds showed significant improvement in blood pressure control or renal function, but few were cured. In only one transplant kidney was it possible to dilate the stenosis successfully. This patient had a good blood pressure response. It proved impossible to perform the procedure in nine patients (including four transplant kidneys) either because of failure to cross the stenosis with catheter or wire, or failure to dilate the lesion. There were three major complications, all arterial occlusion. One subsequently underwent successful surgery. These results are less favourable than some other published data, though there is no comparable British series.

DIRECT PUNCTURE EMBOLISATION WITH SPRING EMBOLI

A. P. Hemingway and D. J. Allison

Department of Diagnostic Radiology, Hammersmith Hospital, London

Vascular embolisation using occluding spring emboli inserted via a catheter is a well established interventional technique. There are a number of situations, however, in which it may be desirable to embolise a vessel which cannot be selectively catheterised because of its anatomical location, or because a major access route has been closed by previous surgery or proximal embolisation. In these circumstances it may be feasible to puncture the target vessel by a direct percutaneous needle approach using guidance by digital subtraction angiography, ultrasound, or CT, and then insert an occluding spring embolus into the vessel through the needle shaft. A direct puncture embolisation kit for this purpose has been used successfully in several patients and is now available commercially from William Cook Europe. The set consists of a direct puncture embolisation needle from which the central stylet can be removed following percutaneous introduction of the needle and replaced by a delivery stylet which carries an occluding embolus on a fine inner mandril. When the tip of the delivery stylet is in a satisfactory location, withdrawal of the inner mandril releases the spring embolus which adopts its coiled configuration at the desired site of vascular occlusion. A combined liver biopsy and embolisation kit is currently under trial which permits a biopsy to be obtained through a percutaneous sheath and the biopsy tract to be embolised with a spring embolus through the same sheath using the direct needle technique.

VENOUS VERSUS ARTERIAL DIGITAL SUBTRACTION ANGIOGRAPHY

H.-J. Maurer

Department of Radiology, St Josef Hospital—Academic Teaching Hospital, Ruprecht-Karls University, Heidelberg, FRG

The problems of angiography seemed to be solved by the introduction of venous DSA. However, despite the high contrast-medium level as well as the high number of contrast steps the results of venous DSA have not been convincing, particularly in abdominal and renal angiography. According to our clinical experience we apply the following techniques. (1) Peripheral angiography: after conventional angiography, regions of interest are investigated by arterial DSA. In case of a suspected Leriche syndrome or obstruction of both iliac arteries, venous DSA is performed. (2) Abdominal and renal angiography: due to a very similar spatial resolution of the vessels we prefer arterial DSA. (3) Neck vessel angiography: despite the relatively good results obtained by venous DSA, arterial DSA is preferred because small arteriosclerotic lesions can be visualised better using the latter technique.

The risk from these invasive techniques, and from the non-ionic contrast media used, is very small.

A CLINICAL STUDY OF INTRA-ARTERIAL SUBTRACTION ANGIOGRAPHY IN SEVERE PERIPHERAL VASCULAR DISEASE

D. McInerney, K. Maher, D. Bouchier-Hayes and A. Walsh

Department of Radiology, Meath/Adelaide Hospitals and Department of Surgery, St Laurence's Hospital, Dublin

From a series of 530 patients attending a specialist clinic for peripheral vascular disease (PVD), 312 had conventional angiography. Eighty-nine patients were selected for intra-arterial subtraction angiography as conventional studies did not provide adequate information for clinical management. This was mainly due to multiple vessel blockages and diminished, slow flow rates. The examination was done as an out-patient procedure and there were no complications. Studies enabled a clinical decision to be made in all cases. There was excellent correlation with operative findings in the 65 patients who underwent surgery. Intra-arterial subtraction angiography has a useful role in studying selective patients with severe PVD.

THE REPRODUCIBILITY OF QUANTIFYING THE DEGREE OF STENOSIS USING DIGITAL FLUOROGRAPHY

P. C. Jackson, H. Key, *E. Thomas, *W. D. Jeans and *E. Rhys Davies

*Departments of Medical Physics and *Radiodiagnosis, Bristol and Weston Health Authority*

The use of digital fluorography and the subsequent subtraction process gives an opportunity to quantify the degree of stenosis in many arterial investigations. In particular, this technique is providing a valuable and near real-time method for assessing interventional techniques. Since the subtraction process can be accomplished by several methods and by different personnel, an assessment has been performed of the inter- and intra-observer reproducibility of quantifying the degree of stenosis using matched temporal filtering and integrated mask-mode subtraction. The problems of obtaining reproducible results are discussed.

COMPARATIVE TESTING OF GRUNTZIG BALLOON DIAMETERS AND BURSTING PRESSURES

J. H. L. Henson, W. D. Jeans, F. J. Newham, C. Paice and A. Blakeborough

Departments of Radiodiagnosis and Civil Engineering, University of Bristol

Balloon catheters supplied by three manufacturers were tested in the Department of Civil Engineering of the University of Bristol. An apparatus was built to allow a balloon to be viewed in three planes simultaneously. The balloons were mounted in a water bath with a thermostatically controlled temperature of 37°C and were inflated to a known pressure using a 20 ml syringe and a calibrated diaphragm pressure transducer. Measurements of the diameters reached were made from photographs taken during the tests, and adjusted for magnification factors. Twelve catheters were examined using an identical series of tests designed to assess the maximum diameter reached, the relation of diameter to distension pressure and multiple inflations and deflations, and the pressure at which the balloon burst. It was found that there was a difference in performance of the products of three manufacturers as shown.

Manufacturer	%Variation in maximum compared with stated diameter	Bursting pressure compared with maximum recommended pressure
A	96–234	63–75
B	93–107	139–157
C	107–142	100–175

Multiple inflations and deflations made no difference to maximum size or to bursting pressure.

Proceedings of The British Institute of Radiology

Obstetrics and Gynaecology

Chairman: Dr H. Nunnerley

Assessment of placenta praevia by MRI, by Dr M. C. Powell, Dr J. H. Buckley, Professor B S. Worthington, H. M. Price and Professor E. M. Symonds

The prognostic significance of antenatally diagnosed urological abnormalities, by Dr H. S. Andrews, Dr J. B. Witcombe, Mr R. D Pocock, Dr P. J. Berry and Dr J. D. Frank

The low-intensity band on spin-echo images of the uterus—a morphological and clinical study, by Professor B. S Worthington, Mr M C. Powell, Dr C. Womack, Dr J H. Buckley and Professor E. M Symonds

The role of MRI in the assessment of carcinoma of the cervix: Mr M. C. Powell, Dr J. H. Buckley, Professor B. S. Worthington, M. L. Wastie and Professor E. M Symonds

Practical MRI in carcinoma of the cervix, by Dr J. D. Spencer, Dr A. W. L. Leung, Dr A. K Dixon and Dr I. D Hill

The role of MRI in the assessment of gestational trophoblastic neoplasia, by Professor B. S. Worthington, Mr M. C. Powell, Dr J. H. Buckley and Professor E. M. Symonds

ASSESSMENT OF PLACENTA PRAEVIA BY MAGNETIC RESONANCE IMAGING

M. C. Powell, J H. Buckley, B. S. Worthington, H. M. Price, E. M. Symonds

Department of Human Morphology, University of Nottingham

The role of MRI in obstetrics is currently under investigation. Maternal anatomy is well demonstrated, excellent soft-tissue contrast being a major advantage of the technique. Using spin echo sequences with long repetition times (TR) and medium or long echo delay times (TE), T_2-weighted images are obtained. The resulting images show the placenta to have a high signal, in contrast to the surrounding tissues The cervix, with the same sequence, has a distinctive trilaminar appearance, permitting ready identification of the internal os. Localisation of the placental site and the relationship of the placental lower edge to the internal os can be assessed accurately.

It is generally accepted that ultrasound examination of the posterior low lying placenta is difficult. A comparative study of 30 women with an ultrasound diagnosis of placenta praevia was undertaken. The MRI findings indicated that in seven cases there had been an overestimation, on ultrasound, of the degree of praevia. The alteration in management consequent on the MRI findings led to a reduction in hospitalisation and, in one case, an alteration in management with regard to Caesarean section. Magnetic resonance imaging will, therefore, be a useful adjunct to ultrasound in the imaging of the difficult placenta praevia

THE PROGNOSTIC SIGNIFICANCE OF ANTENATALLY DIAGNOSED UROLOGICAL ABNORMALITIES

H S. Andrews, *J. B. Witcombe, †R. D Pocock, †P. J. Berry and †J. D. Frank

*Department of Radiodiagnosis, Bristol Maternity Hospital, *Department of Radiodiagnosis, Gloucester Royal Hospital and †Departments of Paediatric Urology and Pathology, Royal Hospital for Sick Children, Bristol*

The detection of fetal abnormality by ultrasound is now routine Urological abnormalities are second only in frequency to those of the central nervous system

Twenty-eight cases of urological abnormality were diagnosed antenatally in a 2-year period These abnormalities were detected by the routine use of antenatal screening in two main centres Seven of the 28 pregnancies were terminated prior to 26-weeks' gestation as a result of the ultrasound findings: lethal urological abnormalities were found in each case Of the remaining 21, four died of renal failure post-natally Fifteen of the 17 babies who are alive and well had an ultrasound scan prior to 24-weeks' gestation. Only one of these revealed the abnormality. In the remaining patients the abnormality was first detected after 28 weeks

From this study two distinct groups emerge first, a bilateral abnormality diagnosed prior to 24 weeks, and almost certain to be lethal; second, an abnormality, which has a good prognosis, detected in the third trimester where there has been a normal early scan This knowledge obviates the need for interventional procedures such as antenatal surgery in late pregnancy.

THE LOW-INTENSITY BAND ON SPIN-ECHO IMAGES OF THE UTERUS: A MORPHOLOGICAL AND CLINICAL STUDY

B S. Worthington, M. Powell, C Womack, J Buckley and E. M. Symonds

Department of Academic Radiology, Queen's Medical Centre, Nottingham

When the uterus is imaged using spin-echo sequences with a relatively long TR (*e g* TR 2000 ms, TE 80 ms), three distinct layers can be identified A central high intensity area corresponding to the endometrium is separated by a low intensity band from the main body of the myometrium which has an intermediate intensity This low intensity band is of variable thickness in normal subjects and can represent up to half of the width of the myometrium It always abuts on the high signal zone of the endometrium and can be seen to extend down into the cervix It has been suggested that this band could represent the stratum basale of the endometrium but we present evidence that it conforms to a compacted layer of muscle just beneath the endometrium. In 15 patients with proven endometrial adenocarcinoma, an excellent correlation was found between the depth of myometrial invasion as assessed by MRI when it was compared with measurement at histology In this regard, thinning or breach of the low intensity band is a useful sign in defining whether tumour invasion of the myometrium has occurred

THE ROLE OF MAGNETIC RESONANCE IMAGING IN THE ASSESSMENT OF CARCINOMA OF THE CERVIX

M. C Powell, J. H. Buckley, B. S. Worthington, M. L. Wastie and E. M. Symonds

Department of Human Morphology, University of Nottingham

Carcinoma of the cervix is the second commonest gynaecological malignancy The incidence is increasing. The mean age of patients with this disease is lower than that of patients with the other malignant neoplasms of the female genital tract. In early disease the distortion of anatomy is well demonstrated by MRI, particularly in the sagittal plane. Additionally, the malignant change results in alteration of signal due to an increase in the T_2 relaxation time This signal abnormality is best seen on T_2-weighted spin echo and on short-TI inversion recovery (STIR) sequences. In more advanced and recurrent disease, the inversion recovery sequence with a long inversion time (TI) provided particularly good contrast between fat and invasive tumour. All patients had CT scans performed and the results were compared with the MRI findings We have found MRI to be the more sensitive method of assessing Stage 1 and 2 disease in comparison with CT In advanced disease the results of MRI and CT were comparable.

PRACTICAL MAGNETIC RESONANCE IMAGING IN CARCINOMA OF THE CERVIX

J D Spencer, A. W. L. Leung, *A. K. Dixon and †I. D. Hill

*Scanner Centre, Mount Vernon Hospital, Northwood, Middlesex, *Department of Radiology, University of Cambridge and †Division of Computing and Statistics, Clinical Research Centre, Harrow, Middlesex*

The 0.5 T superconducting MR system installed at Mount Vernon Hospital is a standard system supplied with a range of imaging sequences Of these sequences, only eight (five spin-echo and three inversion-recovery) provide contiguous multislice images suitable for the routine pelvic imaging of a large number of patients However, each of these eight sequences can be varied by increasing the repeat time from 2.0 to 5.0 s and increasing the number of averages from 1 to 16. With a 256 matrix, imaging times can therefore vary from 8 min to 5 h. This project was undertaken to establish optimum imaging factors for pelvic MR within the practical constraint of a 1 h total study time, bearing in mind that more than one imaging sequence may be needed for each patient.

A series of multislice images of a number of patients with newly diagnosed or recurrent cervical carcinoma were obtained with increasing acquisition times for each of the five spin-echo sequences and three inversion-recovery sequences. The images so obtained were assessed independently by three radiological observers and scored for contrast, resolution and noise The results were analysed using a technique previously described (Spencer & Hill, 1979) and the mean scores for each image recorded. The results are presented for each type of imaging sequence with different repeat times and number of averages.

REFERENCE

SPENCER, J. D. & HILL, I. D, 1979 Imaging factors for xeroradiography of the extremities *British Journal of Radiology*, *52*, 51–55.

THE ROLE OF MAGNETIC RESONANCE IMAGING IN THE ASSESSMENT OF GESTATIONAL TROPHOBLASTIC NEOPLASIA

B. S Worthington, M. Powell, J. Buckley and E. M. Symonds

Department of Academic Radiology, Queen's Medical Centre, Nottingham

Molar pregnancy is rare; the hydatidiform variant has an approximate incidence of 1 in 300 pregnancies in the UK It is important that the uterus be fully evacuated because of the possibility that any tissue left behind might give rise to a choriocarcinoma by malignant transformation While the diagnosis of molar pregnancy is readily made on ultrasound, the plane of demarcation between the mole and the uterine wall is not well shown In three complete and two partial molar pregnancies, T_2-weighted spin-echo images showed clearly the vesicular character of the pathological tissue and its high signal allowed it to be clearly separated from the uterine wall In addition, areas of haemorrhage were identified as regions of high signal on T_1-weighted inversion-recovery images. The clear separation between molar tissue and uterine wall is of great significance because it indicates that macroscopic invasion of the myometrium will be recognisable, and the high signal from molar tissue on spin-echo sequences could be used to confirm recurrence of a mole if HCG titres rose after evacuation Magnetic resonance imaging has also been shown to be useful in assessing the bulk and pelvic spread of recurrent uterine choriocarcinoma

Miscellaneous Radiodiagnosis

Chairman: Dr P. Wilde

The advantages of CT over conventional radiology in monitoring the treatment response of lytic bony metastases, by Dr E. A. Bellamy, Dr D. Nicholas, M Ward, R. C. Coombes, T. J. Powles and Dr J. E. Husband
Rhabdomyosarcoma of childhood, by Dr S. Thurairajasingam
The application of real-time ultrasound in intensive care, by Dr J. E. Boultbee, Dr C. Marshall and Dr W. Kox
The value of oesophageal transit tests in the investigation of patients with chest pain, by Dr K. S. Channer, Dr P. C Jackson and Dr J. P Virjee
^{111}In labelled leucocyte imaging—a review of 150 studies, by Dr M. Yamoto, Dr W. N Tauxe, Dr L. Gumerman and Dr H Klein
Potential non-cardiac applications of cine CT, by Dr M. R. Rees, Dr S Flicker; Dr W. J Eldredge, Dr R. M MacMillan and Dr D L Clark

THE ADVANTAGES OF COMPUTED TOMOGRAPHY OVER CONVENTIONAL RADIOLOGY IN MONITORING THE TREATMENT RESPONSE OF LYTIC BONY METASTASES

E. A. Bellamy, D Nicholas, M. Ward, R. C. Coombes, T. J. Powles and J. E. Husband

Royal Marsden Hospital and Institute of Cancer Research, Sutton, Surrey

Full skeletal survey, localised radiographs and CT examinations were compared with clinical assessment in the evaluation of treatment response of bony metastases in 20 patients with carcinoma of the breast The CT assessment was based upon both visual appraisal of the images and a quantitative measurement of mean electron density within the abnormal area. Results are presented which indicate that conventional radiology (skeletal survey and localised view) compares poorly with clinical assessment, agreeing in only 35% and 50% of cases, respectively However, CT concurs with the clinical assessment in 65% of patients, particularly with respect to healing (86%) Furthermore, in this study CT predicted the effect of treatment in six additional patients which has been confirmed on retrospective follow-up assessment It is suggested that the use of skeletal surveys in monitoring treatment response is limited and that for critical evaluation of treatment effects, CT scanning should be the method of choice.

RHABDOMYOSARCOMA OF CHILDHOOD

S. Thurairajasingam

Royal Manchester Children's Hospital, Pendlebury, Manchester

This is a study of 38 cases (23 males, 15 females) of rhabdomyosarcoma treated at the Royal Manchester Children's Hospital over the last 10 years Four were under 1 year old. Others were fairly evenly distributed from 1 to 15 years. Sites of origin extended from temporal region to the foot Local bony erosion was seen in seven (18%). Distant spread—11 (29%) developed metastases· (a) bony deposits, three; (b) nodal deposits, six including two of (a); (c) pulmonary deposits, four. Lung and bones were not simultaneously involved by metastases Other chest lesions: pneumonia is common in these children. Thirteen had one or more attacks, three by opportunistic invaders. Pleural effusions were seen in four One was associated with pneumonia, one with pulmonary metastases In the other two, pleura was directly infiltrated. Both had ascites Heart. one had reversible cardiac failure with pulmonary oedema Progressive cardiomegaly occurred up to death in another. This seemed to be a drug effect. There was no other radiologically demonstrable complication of treatment Prognosis has improved in recent years; 17 are alive and well Twelve, including two of three recurrences, died Nine were lost for follow up.

THE APPLICATION OF REAL-TIME ULTRASOUND IN INTENSIVE CARE

J. Boultbee, C. Marshall and W. Kox

Charing Cross Hospital, Fulham, London

Diagnostic ultrasound has many applications in the intensive care ward, particularly in identifying fluid collections in the abdominal cavity, the pleura and the pericardium. There are logistic problems in scanning the abdominal organs in patients on life support, but the mobility and flexibility of modern real-time scan heads have largely overcome these problems Where the combination of real-time ultrasound and plain-film radiography of the chest and abdomen has failed technically or leaves areas of doubt, a CT examination seems mandatory

The results of 58 patients who were examined on the intensive care ward are reviewed. In 37 patients, multiple or single fluid collections were found ultrasonically Twenty patients had aspiration of the fluid, often in more than one site; six patients had surgical intervention, another two patients had findings confirmed at the post-mortem examination Twenty-one patients where no fluid was found have been reviewed and the implications of a negative examination are discussed.

THE VALUE OF OESOPHAGEAL TRANSIT TESTS IN THE INVESTIGATION OF PATIENTS WITH CHEST PAIN

K. S. Channer, P. C. Jackson and J. P Virjee

Department of Cardiology and Radiodiagnosis, Bristol Royal Infirmary

Oesophageal disease may cause chest pain indistinguishable from angina and it is thought to account for the pain in half the cases of angina with normal coronary angiograms. The aim of this study was to assess whether simple oesophageal transit tests could discriminate between patients with chest pain with and without coronary artery disease

Twelve patients (eight female), mean age 53.3 (range 40–69) years, investigated for angina were found to have normal coronary angiograms. These patients were age and sex matched with 12 patients who had angina and significant stenoses of > 50% diameter on coronary angiography. Oesophageal function was assessed by barium swallow examination and by timing the transit through the oesophagus of both a radioactively labelled water bolus (WTT) and barium-sulphate filled capsules (CTT). Oesophageal peristalsis, as judged by prone barium swallow examination, was abnormal in three patients (25%) with normal angiograms and six patients (50%) with abnormal angiograms. Median WTT was 13.6 (range 7.75–100) s in patients with normal angiograms and 16.4 (range 7–100) s in patients with abnormal angiograms ($P = 0.38$). Median CTT was 300 (range 9–300) s in patients with normal angiograms and 155.5 (range 9.25–300) s in patients with abnormal angiograms ($P = 0.07$).

In conclusion, resting abnormalities of oesophageal function were equally common in patients with angina-like chest pain with normal and abnormal coronary angiograms.

INDIUM-111 LABELLED LEUCOCYTE IMAGING: A REVIEW OF 150 STUDIES

M. Yamoto, W. N. Tauxe, L. Gumerman and H. Klein

School of Medicine, University of Pittsburgh, Pennsylvania, USA

One-hundred and fifty studies (144 cases) of ^{111}In labelled leukocyte scan were retrospectively analysed. The results were correlated with other imaging modalities including clinical, laboratory, surgical and pathological findings. Of the cases, 36% were immunocompromised hosts and 31% were organ transplant patients. There were 79 abnormal studies. Of these, 59 studies had abnormal uptake in the abdomen, 46% of them were associated with abscess or infectious process, 37% had non-infectious causes and 7% were non-inflammatory (bleeding, malignant tumour). Intense uptake greater than in spleen was usually associated with abscess, but there was an exception. There were 33 studies with lung uptake. Only 30% of them were due to infection. Intensity or size of uptake could not distinguish infection from other processes. It was concluded that a variety of non-infectious and non-inflammatory processes accumulate ^{111}In leukocyte and differentiation from abscess or infectious causes is often difficult.

POTENTIAL NON-CARDIAC APPLICATIONS OF CINE COMPUTED TOMOGRAPHY

M. R. Rees, S. Flicker, *W. J. Eldredge, R. M. MacMillan and D. L. Clark

*Killingbeck Hospital, Leeds and *Deborah Heart and Lung Center, Brown Mills, USA*

Cine CT has the potential to investigate function in a wide variety of organ systems. Early experience has shown that it is possible to construct time–density curves from contrast flow in normal and abnormal lung. Three cases of lung collapse were studied and rapid contrast flow through the abnormal lung demonstrated; time of contrast flow could be compared with flow through the heart and normal lung tissue. This method has potential application in the investigation of the physiology of lung collapse. Local pulmonary ventilation was investigated by cine CT using non-radioactive Xe in five normal male subjects, demonstrating differences in ventilation between apex and base of lung (Murphy et al, 1985).

Renal contrast flow has been clearly demonstrated by acquiring images in a rapid timed mode (up to 58 ms intervals). Flow from the aorta through the renal artery to the renal cortex and into the renal vein can be differentiated and measured. Flow in different areas of renal cortex can be compared. Differences in flow between kidneys may also be shown. Cine CT can be used to demonstrate upper airway dynamics; eight contiguous scans of the upper airway are taken at 0.6 s intervals during normal respiration. Replaying these scans in a closed loop mode allows the evaluation of normal and abnormal airway movement (Ell et al, 1985).

Joint motion can also be studied; normal radio-ulnar joint movement can be demonstrated, with the possibility of investigating abnormal joint movement by this method.

Although the scanner has a lower spatial resolution at present than many conventional CT scanners, improvements in resolution are being developed. Even at present the ability to acquire rapid scans represents a considerable advance in patient throughput, and loss of spatial resolution is often compensated by elimination of movement artefact. The whole chest can be scanned in 15 s and give good sagittal reconstruction. This was found to be useful in the investigation of aortic disease, particularly coarctation of the aorta which could be localised. It is concluded that cine CT has wide non-cardiac applications.

REFERENCES

Ell, S. R., Jolles, H., Rees, M. R., Keyes, W. D., Galvin, J. R., 1985. The role of cine CT in non-fixed upper airway disease. *Presented at the Society of Thoracic Radiology, Miami, USA, March*

Murphy, P., Nicewicz, J. T., Moore, R., Flicker, S., Wolfe, P., Welsh, J., Rees, M. R. & Clark, D. L., 1985. Local pulmonary ventilation using non-radioactive xenon enhanced ultra fast computed tomography. *Presentation to the American Society of Thoracic Medicine, New Orleans, USA, November*

Proceedings of The British Institute of Radiology

Musculoskeletal Radiology Update

Chairman: Dr I. Watt

Developments in rheumatology—the interface between physicians and radiologists, by Dr P. A. Dieppe
Prognostic radiology for osteoarthritis, by Professor L Solomon
The radiographic and scintigraphic features of diabetic osteoarthropathy, by Dr D. J. Tawn, Dr J. P O'Hare, Dr I. Watt, Dr P. A Dieppe and R. J. M. Corrall
$^{99}\mathrm{Tc}^{m}$ HMDP bone scanning in osteoarthritis—a predictor of joint progression, by Dr C. W. Hutton, Dr I. Watt and Dr P A. Dieppe
CT in patients with low back pain and sciatica—an analysis of 250 patients, by Dr J. L. G. Thomson
CT of the post-operative lumbar spine: is enhancement always necessary? by R. P. Bannon and Dr A. K. Dixon
The changes in the intervertebral disc after chemonucleolysis demonstrated by MRI, by Dr M. J. Gibson, Dr J H. Buckley, Dr R. R. Mawhinney, Dr R. C. Mulholland and Professor B. S. Worthington
MRI of syringomyelia using surface coils, by Dr M. H. Guilleux, Dr G. M Bydder and Professor R. E. Steiner

DEVELOPMENTS IN RHEUMATOLOGY: THE INTERFACE BETWEEN PHYSICIANS AND RADIOLOGISTS

P. Dieppe

Bristol University

Changing patterns of populations and disease prevalence in the UK have led to a relative increase in the importance of rheumatic diseases in health care. Rheumatology is also a growth industry Over the last decade several new joint disorders have been described, new therapeutic modalities introduced, and sophisticated investigative procedures developed. However, diagnosis and assessment of disease progression still depend largely on clinical examination and the plain radiograph

Inflammatory polyarthritis can now be subdivided into several types on the basis of serological and other markers Prognosis seems to vary in the different groups. Many centres are now trying to match these serological subsets with radiological changes. Several drugs appear capable of altering disease progression, and prospective long-term studies of radiographic change are also being undertaken. Methods of standardising the reporting of radiographic changes and of measuring progression need to be developed.

Osteoarthritis also includes many disease subsets, and a number of factors which may alter disease expression or outcome can now be identified. Radiological chondrocalcinosis is an example of a phenomenon sometimes associated with a different pattern of disease which may respond to different therapy. Chondrocalcinosis and pyrophosphate arthropathy are reviewed as an example of a developing area of rheumatology depending on an interface between physician and radiologist.

PROGNOSTIC RADIOLOGY FOR OSTEOARTHRITIS

L. Solomon

Department of Orthopaedic Surgery, Bristol Royal Infirmary

Evidence is accumulating to support the hypothesis that osteoarthritis (OA) represents a collection of disorders that have a final common pathway in the progressive articular destruction which has come to be regarded as the hallmark of the disease The "subsetting" of OA in this manner is seen as a first step to elaborating a model of pathogenesis It is posited here that the subsets also have different prognostic implications For example, "hypertrophic OA" is associated with good bone formation, active remodelling tends to stabilise the failing joint and articular destruction may be delayed for many years "Atrophic OA" shows more rapid progression and responds poorly to conservative treatment. The recognition of these trends and an assessment of bone-forming capacity on the part of the host tissues are important in planning management

The prognostic criteria for OA of the hip have been evaluated in over 200 patients admitted to hospital for hip replacement. These findings are described.

THE RADIOGRAPHIC AND SCINTIGRAPHIC FEATURES OF DIABETIC OSTEOARTHROPATHY

D. J. Tawn, J. P. O'Hare, I. Watt, P. A. Dieppe and R. J. M. Corrall

Institute of Orthopaedics, Oswestry, Shropshire

The clinical, radiographic and scintigraphic features of the osteoarthropathy in the feet of 34 diabetic patients known to have a peripheral neuropathy are being studied The type and severity of the neuropathy have been assessed by peripheral nerve conduction velocities, tests of autonomic function, and vibration perception thresholds Radiographs and blood pool and late phase $^{99}\mathrm{Tc}^{m}$-HMDP bone scans of both feet and ankles were performed A blood biochemistry profile is available on each patient Initial results indicate that the type and severity of the bone and joint lesions depend upon the type and severity of the peripheral neuropathy and the state of the vascular supply to the foot. Examples of the various lesions of diabetic osteoarthropathy are presented. Scintigraphy is the best indicator of disease activity. Abnormal scintigraphy with normal radiographs indicates activity Abnormal radiographs with negative scintigraphy suggests quiescence.

TECHNETIUM-99m HMDP BONE SCANNING IN OSTEOARTHRITIS: A PREDICTOR OF JOINT PROGRESSION

C. W. Hutton, *I. Watt and P. A. Dieppe

*Departments of Rheumatology and *Radiology, Bristol Royal Infirmary*

Investigating the cause and evaluating therapy in osteoarthritis is hampered by the inability to predict the disease's evolution and to measure its progression Radiographs can only define the anatomical abnormality. Radionuclide bone scanning depends on radionuclide uptake, and so may reflect a pathophysiological process in a manner that can be quantified. We studied its significance in generalised nodal osteoarthritis (GNOA), a possible subgroup of osteoarthritis.

A hand radiograph and a 4 h gamma-camera ^{99}Tc^{m} HMDP scan image were obtained in 33 patients with GNOA. A single observer, unaware of patient identity and the complementary radiograph or scan image, evaluated the films and scored each joint for abnormality on a 0–3 scale. Fourteen patients were then prospectively followed for 3–5 years and the scan and radiograph repeated. These were scored in a similar manner. The pattern of joint abnormality could then be assessed objectively and the possible predictive value of that pattern on the subsequent progression of osteoarthritis evaluated. In the initial study of 33 patients, the pattern of joint involvement on scan showed marked discrepancy compared with the radiograph. Of a total of 1054 joints, 20% were abnormal on the radiograph and scan, 12% on the radiograph alone and 8% on scan alone. At follow-up of 14 patients 44% of joints abnormal on scan showed progression and 52% remained unchanged. In contrast, only 10% of joints normal on initial scan showed progression; 88% remained unchanged. The remainder of joints showed regression. Of joints abnormal on scan, but normal on the radiograph, 70% progressed, whereas 14% of joints abnormal on the radiograph, but normal on scan, progressed. Some joints initially abnormal on scan became normal at follow-up.

It appears that scanning predicts the subsequent evolution of radiographic abnormality. It demonstrates the changing activity of an apparently phasic disease process. Joints are initially abnormal on scan, the radiographic signs then develop, and as changes on the scan diminish, no further radiographic change occurs. ^{99}Tc^{m} HMDP bone scanning may therefore provide a means of assessing osteoarthritis. Further understanding of the mechanisms of uptake may give insight into the aetiology of the disease.

COMPUTED TOMOGRAPHY IN PATIENTS WITH LOW BACK PAIN AND SCIATICA: AN ANALYSIS OF 250 PATIENTS

J. L. G. Thomson

Neuro-X-ray Department, Frenchay Hospital, Bristol

At present 219 consecutive patients having CT scans for clinical low backache and sciatica have been reviewed. Of these examinations, 144 were carried out on an outpatient basis, and 75 from the wards. Eighty-seven of the patients were treated by operative surgery; 50 of these had been investigated by CT alone and the operative findings agreed with the written CT report. A further 21 patients had CT and radiculography, and operation confirmed the findings. A few others showed mild discrepancies which are discussed. Some of the non-operated cases were treated by epidermal injections or chymopapain injection.

COMPUTED TOMOGRAPHY OF THE POST-OPERATIVE LUMBAR SPINE: IS ENHANCEMENT ALWAYS NECESSARY?

R. P. Bannon and A. K. Dixon

Department of Radiology, Addenbrooke's Hospital, Cambridge

Forty-five patients who had previously had a laminectomy were referred for CT in order to elucidate the cause of new, continuing, or recurrent clinical problems. The patients were randomly allocated to one of three groups. In one group of 15 patients, CT was performed both before and after a bolus of 50 ml intravenous contrast medium (16 g I); a second group received 100 ml (32 g I). In the third group no contrast medium was given. In each patient an attempt was made to characterise the nature of any abnormal soft tissue from the CT appearances. Particular effort was made to differentiate between disc material and fibrosis. The effects of the different doses of contrast medium are discussed. In some patients there was no significant CT abnormality, here the administration of contrast medium was superfluous. In most patients the pre-contrast CT features strongly pointed towards either fibrosis or disc material; here enhancement merely confirmed these features. Contrast medium is, however, of great value in that minority of patients in whom the initial CT findings are equivocal.

THE CHANGES IN THE INTERVERTEBRAL DISC AFTER CHEMONUCLEOLYSIS DEMONSTRATED BY MAGNETIC RESONANCE IMAGING

M. J. Gibson, J. Buckley, R. R. Mawhinney, R. C. Mulholland and B. S. Worthington

University Hospital, Nottingham

Chemonucleolysis with the enzyme chymopapain is an established treatment for sciatica secondary to intervertebral herniation/protrusion. This is a prospective study of the serial changes in the MRI appearance of the intervertebral disc after injection of chymopapain. Fourteen patients have been studied after single-level chemonucleolysis and the results compared with a control group of 15 discs in five patients having diagnostic discography without enzyme insertion. A consistent pattern of gradual loss of signal from the nucleus pulposus culminating in a complete loss of nuclear signal was seen in all cases after chemonucleolysis. The rate at which this change occurred varied between 6 and 18 weeks. Transitory minor end-plate changes were present in five patients, probably representing a mild chemical discitis. No similar changes were seen in the discography group.

MAGNETIC RESONANCE IMAGING OF SYRINGOMYELIA USING SURFACE COILS

M. H. Guilleux, G. M. Bydder and R. E. Steiner

Department of Diagnostic Radiology, Hammersmith Hospital, London

The study was designed to assess the ability of MRI to diagnose syringomyelia, evaluate its extent and detect associated abnormalities. Twenty-nine patients referred with clinical features suggestive of syringomyelia were examined using surface coils on a 0.15 T MRI system. The pulse sequences used included spin-echo ($SE_{544/44}$ and $SE_{1500/80}$) as well as inversion-recovery ($IR_{1500/500/44}$). Gadolinium-DTPA was used in two cases. A comparison was made with myelography, CT and metrizamide CT studies.

Syringomyelia was identified in 12 cases as a cystic intramedullary lesion with well defined margins. The cord was widened in seven cases but was of normal size in five. The upper extent of the cavity was well demonstrated in each case, but the lower extent was less well seen in seven cases due to the presence of scoliosis and insufficient length of the surface coil. Associated abnormalities were found in all cases (Chiari I malformation, vertebral injury, tumour). An expanded cord was demonstrated with myelography in six of 17 cases. Metrizamide CT showed a cyst in two of eight cases (after delayed study in one case). Among the remaining 17 patients whose MRI scans afforded no diagnosis, syrinx was not demonstrated with any other technique.

Proceedings of The British Institute of Radiology

Modern Mould Room Techniques

Chairman: Dr N. K. Gupta

Setting up and managing a mould room, by Mr G. K. Lowndes
One approach to the production of a light-weight shell, by Mr F. A. Stanton
The problems of CT scanning in a shell, by Ms J. E. Clinkard
3-D tissue compensation, by Mr R. E. Hutchings
Do we need abdominal shells for conformation therapy? by Dr T. J. Davy and A. T. Tate
Facial prostheses. A small corner of the mould room, by Mrs D. Studd

SETTING UP AND MANAGING A MOULD ROOM

G. K. Lowndes

Radiation Physics Section, Department of Medical Physics and Clinical Engineering, Weston Park Hospital, Sheffield

The primary function of the mould department is to provide shells and related devices to obtain reproducible beam direction, beam definition, compensation and attenuation results. These must be applicable to local conditions and, for this reason, there are probably as many variations in the final product as there are departments in existence.

In initiating a new department, primary considerations would include:

(i) the requirements and expectations of the consultant therapy staff;
(ii) the energies and movement capabilities of the available treatment equipment;
(iii) the availability of trained personnel or the acquisition of training for existing staff possessing relevant aptitude.

The accommodation should be sited with easy access to the treatment department, the simulator and the treatment planning room. It needs to be of adequate size and equipped with tools and facilities according to the materials to be employed. In a small department, a single work room (possibly with a curtained or partitioned patient area) employing one technician, producing a few simple but nonetheless effective devices, may suffice. However, in the teaching hospital situation, with ongoing development as new materials, equipment and technical skills evolve, and to allow for greater complexity and increased throughput of patients, a suite of rooms with specialised areas may prove more appropriate.

At the outset, a correctly structured operational policy relating to logical sequences in production and patient management will ensure smooth co-operation with related areas and inspire a reassuring atmosphere in the patient.

ONE APPROACH TO THE PRODUCTION OF A LIGHTWEIGHT SHELL

F. A. Stanton

Christie Hospital & Holt Radium Institute, Manchester

The particular needs of different radiotherapy centres necessitate differing designs and methods of construction of beam direction shells. However, certain requirements are fundamental for any shell, in that it must confine the planned treatment to a defined volume, by virtue of its own accuracy.

This presentation outlines the method of construction of a shell as practised at the Christie Hospital. By discussion of the various alternatives, the choice of techniques and materials is explained.

Several materials are available for taking impressions. Plaster of Paris bandage is preferred because of its ease of use and economy. A lightweight "UVEX" shell is used, which is not secured to a base board, as patients feel less claustrophobic, and any movement of the shell is easily noticed and corrected. Treatment volume localisation and verification is achieved by taking radiographs with various markers fixed to the shell. This enables decisions regarding volumes to be made without the requirement for simultaneous presence of patient and doctor at a treatment simulator facility. A contour table is used to give an accurate outline of the treatment plane, which is required for planning. The treatment fields may then be transferred to the shell with the aid of beam simulation templates. Any necessary tissue compensation may be achieved by a combination of "in the beam" wedges and/or surface wax compensators; the latter, although resulting in loss of skin sparing, are accurately placed on the shell. The treatment ports are then cut out, leaving a central "plate" line and field centre. The shell is then completed by marking the setting-up factors on the shell.

THE PROBLEMS OF COMPUTED TOMOGRAPHIC SCANNING IN A SHELL

J. E. Clinkard

Cookridge Hospital, Leeds

To enable information from a CT scan to be used directly for radiotherapy treatment planning of lesions of the head and neck, the patient must be scanned in the treatment shell. The sites chosen for investigation were antrum, ethmoid and nasopharynx. Lesions in these areas would normally be investigated by diagnostic CT scanning prior to radiotherapy treatment planning. The aim was to produce satisfactory scans with the patient in the treatment position so that the information could be used directly for planning purposes. The main problems encountered were in adapting the existing shell and head-rest to reduce artefacts on the CT scan, and in positioning the patient in order to obtain a scan showing the whole outline of the head.

Having obtained a suitable scan in the plane of the intended treatment, it was used to provide the patient outline and target volume information. Outlines of CT scans from a Philips Tomoscan 310 have been produced on both the Philips Independent Viewing Console, and an AECL Theraplan System, the latter enabling field positioning and treatment planning to proceed directly. The presence of a shell on the scan can cause problems in producing an automatic outline of the patient. Markers placed on the shell as reference points may be obliterated by the drawing of the patient outline. This can cause problems in relating the outline to the shell.

The technique has enabled a single series of CT scans to be used to provide both diagnostic information and information leading to direct treatment planning.

THREE-DIMENSIONAL TISSUE COMPENSATION

R. E. Hutchings

Department of Medical Physics, Norfolk & Norwich Hospital, Norwich

This system presents a method of three dimensional beam attenuation to enable a particular isodose distribution to be accurately positioned within a patient contour. Contours are transposed from a beam direction shell using a digital contour table which allows contour outlines to be entered into a computer to construct a three dimensional "wire frame" image. Also contained within the image is other relevant information such as beam outlines, central axis and low-tolerance areas. On completion of the data input, the computer will display the wire frame image, which can be rotated in any direction to enable otherwise hidden areas to be observed and, if necessary, receive correction

Any single contour can be displayed on which a volume could be defined and an isodose level prescribed. The system will then calculate and design the shape of the compensator to enable the prescription to be achieved. A rotating cutting tool attached to a three axis arm will, under computer control, cut a reverse image of the required compensator depth into a high-density polystyrene block. Each compensator, having been cast, is attached to a perspex plate which is accurately positioned in the beam path after the patient has been set up on the treatment machine.

DO WE NEED ABDOMINAL SHELLS FOR CONFORMATION THERAPY?

T. J. Davy and *A. T. Tate

*Medical Physics Department, and *Department of Radiotherapy and Oncology, Royal Free Hospital, London*

In conformation therapy the treatment volume is shaped to match the target volume in three dimensions. Accurate tumour localisation, reproducible patient set-up, durability of reference marks and immobilisation are essential if the technique is to be fully exploited. An effective and economical shell will simplify the attainment of these objectives. At present we rely on a "free" set-up with sagittal, coronal and transverse reference planes marked on the skin, beam films demonstrate reproducibility of set-up and laser positioning lights confirm lack of patient movement. However, this setting-up procedure is time consuming and taxing for the patient. When patient numbers are increased, a well constructed treatment shell will be an important aid. Such a shell will be quickly and economically made, the patient will be able to assume easily his treatment position and the body shape will be fixed and quickly checked. The shell will provide the added advantages of improved immobilisation and set-up reproducibility. With the new generation of conformation therapy machines and automatic planning systems, the setting-up time will become an increasingly important factor in restricting patient throughput. We believe that minimisation of set-up time will prove to be the principal advantage of treatment shells There is a need for quantitative studies to confirm their usefulness.

FACIAL PROSTHESES. A CORNER OF THE MOULD ROOM

D. M. M. Studd

Mould Room, Christie Hospital and Holt Radium Institute, Manchester

Facial disability is a very severe handicap. Despite advances in reconstructive surgery, prosthesis may offer the only answer. There are few centres which have the technical and artistic expertise necessary to produce an excellent prosthesis. Maxillo-facial technologists employed in the larger general hospitals generally undertake this task. Their routine work, like ours, demanding and urgent, creates a situation where the prosthetics have to become subsidiary to the main work of the department concerned A complete prosthesis requires regular renovation and replacement, therefore follow-up is necessary, reducing the time available for teaching, development, and research.

This paper describes:

(a) the techniques of prosthesis production;
(b) the properties which determine the suitability of the materials available;
(c) the psychological aspects, including the need to avoid the generation of unrealistic expectations in new patients,
(d) the methods of retention,
(e) the planning involved with the surgeon and technician before the operation;
(f) the limits of technical achievements in preparation

Each patient presents a different problem, dictating an individual approach. A close liaison between patient and technician can make the work gratifying as well as challenging and absorbing

Proceedings of The British Institute of Radiology

Radiotherapy and Oncology

Chairman: Dr B. T. Hale

CT demonstration of the development of benign thymic enlargement in adult patients after chemotherapy, by Dr C. M. Kissin, Dr J. E. Husband, Dr W. Eversman and Dr D. Nicholas
How does CT scanning contribute to the treatment of cancer of the larynx? by Dr P. J. D. K. Dawes, Dr D. Patrick and Dr K. Hall
Surgery, chemotherapy and whole-abdominal radiotherapy in the management of advanced ovarian carcinoma, by Dr M. J. Minton, Dr G. J. S. Rustin, Dr B. M. Southcott, Dr M. G. Glaser, N. Howard, E. S. Newlands, R. H. J. Begent and K. D. Bagshawe
Stage I malignant teratoma treated by orchidectomy alone—results of a study in the South West, by Dr S. E. Goodman and Dr P. A. Light
Improving radiotherapy for astrocytomas, by Dr C. H. Collis and Dr J. A. Bullimore
Use of various imaging techniques for the localisation of the treatment volume in breast carcinoma, by Dr J. Lovett, Dr J. A. Bullimore, Dr E. C. Whipp, Dr P. H. Stevens, M. Halliwell, Dr H. J. Appleby, C. S. Abbott, D. Coules and T. J. Godden
The use of mitoxantrone as a single agent in the treatment of advanced breast cancer, by Dr M. H. Robinson, Dr K. D. Durrant and Dr A. C. Jones
New radiosensitising drugs, by Dr S. Dische and Dr M. I. Saunders
Changes in helper and suppressor T-lymphocytes following radiotherapy for breast carcinoma, by Dr G. H. Newman, Dr G. J. G. Rees, Dr R. S. J. Jones, E. A. Grove and A. W. Preece
Prostatic ^{125}I implant under ultrasound guidance (a) clinical considerations, by Dr E. C. Whipp and H. Eckert
Prostatic ^{125}I implant under ultrasound guidance (b) physical principles, by Miss H. J. Appleby, Dr M. Halliwell and Mr T. J. Godden
Hyperfractionation in advanced head and neck cancer—results of a randomised clinical trial, by Professor V. Balasundaram, Dr M. S. Vidyasagar and Mr J. G. R. Solomon
Radiotherapy employing three fractions each day over a continuous period of 12 days, by Dr M. I. Saunders and Dr S. Dische
Radiotherapy of advanced head and neck cancer using multiple fractions daily, by Dr D. A. L. Morgan and Mr P. J. Bradley

COMPUTED TOMOGRAPHIC DEMONSTRATION OF THE DEVELOPMENT OF BENIGN THYMIC ENLARGEMENT IN ADULT PATIENTS AFTER CHEMOTHERAPY

C. M. Kissin, J. E. Husband, W. Eversman and D. Nicholas

CRC CT Scanning Unit, Royal Marsden Hospital, Sutton, Surrey

It is recognised that in children the thymus may atrophy during illness and then show regrowth or even "rebound" hyperplasia on return to health. We have demonstrated that this phenomenon also occurs in adults who have been successfully treated with chemotherapy for metastatic testicular tumours. We emphasise that this appearance may falsely simulate disease relapse.

We reviewed the CT scans of 200 patients with testicular tumours. 120 had been treated with chemotherapy for metastatic disease and 80 had Stage I disease and had, therefore, undergone orchidectomy only. Thymic enlargement had occurred in 14 (8.6%) of the patients who received chemotherapy, aged 17 to 39 years. This developed between 3 and 20 months after the commencement of treatment. Serial measurements demonstrated that, while the thymic volume increased substantially, the CT number remained constant. Histological examination of the thymus in one patient supported this finding by demonstrating that the enlargement was a true hyperplasia.

In the control group of 80 patients who did not receive chemotherapy minimal thymic enlargement was noted in one patient only, who had suffered numerous intercurrent infections.

The prognostic significance of the thymic enlargement in these patients is discussed.

HOW DOES COMPUTED TOMOGRAPHIC SCANNING CONTRIBUTE TO THE TREATMENT OF CANCER OF THE LARYNX?

P. J. D. K. Dawes, D. Patrick and K. Hall

Regional Radiotherapy Centre, Radiology and Neuroradiology Departments, Newcastle General Hospital

In 1983 CT scanning was introduced to Newcastle upon Tyne Hospitals. A study was undertaken to assess the value of CT scanning in the planning of radiotherapy treatment of the larynx. Despite the fact that only a 256 matrix image could be used (because the treatment planning VDU would not accept a 512 matrix image), acceptable diagnostic images were obtained in the treatment shells. At the end of 1983, the CT scans were compared with conventional tomographs of the larynx. The conclusion was that for clinical $T_1N_0M_0$ carcinomas of the laryngeal glottis, if the direct laryngoscopy findings of a tumour confined to the vocal cords was confirmed by conventional tomography, CT scanning offered no further information. Fourteen cases treated for $T_1N_0M_0$ carcinoma of larynx in 1983 have a mean disease-free survival of 17 months. One of these patients died from a myocardial infarct at 11 months without evidence of recurrence. No patient in this group had a recurrence. For more advanced glottic carcinomas and all other laryngeal carcinomas, CT scanning offered greater information. Approximately 35% of treatment plans were affected by the CT scan. In 11% of these cases this alteration has probably affected survival. In 1984 a policy of conventional tomography only in $T_1N_0M_0$ glottic carcinomas and CT scanning only in other cases was implemented. The policy appears satisfactory.

SURGERY, CHEMOTHERAPY AND WHOLE-ABDOMINAL RADIOTHERAPY IN THE MANAGEMENT OF ADVANCED OVARIAN CARCINOMA

M. J. Minton, *G. J. S. Rustin, B. M. Southcott, M. G. Glaser, N. Howard, *E. S. Newlands, *R. H. J. Begent and *K. D. Bagshawe

*Radiotherapy and *Medical Oncology Departments, Charing Cross Hospital, London*

A pilot study on 36 women has been undertaken to determine the feasibility of giving whole-abdominal radiotherapy after debulking surgery and chemotherapy for Stage III and IV ovarian adenocarcinoma. Chemotherapy consisted of four courses of cisplatinum 100 mg/m^2 alternating with four courses of cyclophosphamide 500 mg/m^2 with folinic acid rescue. Twenty-nine out of 36 (80%) patients were shown at second-look surgery to have $\leqslant 2$ cm residual disease after chemotherapy.

The planned radiotherapy dose was 2400 cGy in 20 fractions over 26 days by the open-field technique and was well tolerated. Three patients failed to complete radiotherapy, two because of progressive disease and one because of vomiting. Myelosuppression was seen but was not treatment-limiting with the WBC nadir of 1.5×10^9/l being reached by 1300 cGy and the platelet count nadir of 45×10^9/l reached by 1400 cGy, but which then plateaued or recovered, despite continuing radiotherapy. Median follow-up time since diagnosis is 26 months and, of 27 patients completing treatment, 17 have relapsed, the majority, 14 out of 17, in the abdomen. The median duration of survival of Stage III patients from completion of treatment was 18 months.

As a result of our experience we are now evaluating whole-abdominal radiotherapy after chemotherapy for patients with no or minimal residual disease in a prospective randomised trial.

STAGE I MALIGNANT TERATOMA TREATED BY ORCHIDECTOMY ALONE: RESULTS OF A STUDY IN THE SOUTH WEST

S. E Goodman and P. Light

Bristol Radiotherapy and Oncology Centre

The South West Testicular Tumour Study Group was established in 1981 to standardise the management of malignant teratoma in the region and to evaluate the results. One-hundred and thirty-four patients have been staged and treated according to the protocol; 71 were apparently clear of disease following orchidectomy (Stage I). Of these, 57 were entered into a programme of close surveillance and 14 for whom this was logistically unsuitable received prophylactic radiotherapy. In the surveillance group 18 patients (32%) had tumour recurrence and were treated with chemotherapy. Thirteen showed complete response, four partial response and one no response. Three patients are now dead. In the surveillance group 90% are alive and free of disease. In the radiotherapy group, four patients (29%) had tumour recurrence and were treated with chemotherapy. Two showed complete response, one partial response and one no response. Two patients have died. Eighty-six per cent are alive and free of disease.

Features of recurrence are discussed. The results indicate that surveillance is effective in the majority of this group of patients. Further analysis is directed towards identification of an "at risk" group.

IMPROVING RADIOTHERAPY FOR ASTROCYTOMAS

C. H. Collis and J. A Bullimore

Radiotherapy Centre, Bristol

More than 100 patients with astrocytomas treated between 1980 and 1983 at the Radiotherapy Centre in Bristol have been reviewed. Initially, patients were treated with 45 Gy in 20 fractions to a generous volume. Latterly, 60 Gy in 30 fractions was given, 30–40 Gy to a large volume, the second phase to a small volume. Of the cases, 80% were high grade malignant astrocytomas (Kernohan and Sayre, Grade III and IV). Survival was increased in those receiving 54–61 Gy compared with those who received 40–48 Gy, with 35% alive at 1 year compared with 25%, but by 2 years only 8% were alive in each group and there is only one longer term survivor. The natural history of the "low grade" tumours was quite different, with 50% still alive, but the numbers were too small to make a comparison between treatments.

In view of the dose-dependent response of high grade tumours, we have assessed the use of implantation with ^{192}Ir. The technique is described and illustrated. Although we had some success, the logistics of it have proved difficult. We are, therefore, now developing further techniques which are outlined.

USE OF VARIOUS IMAGING TECHNIQUES FOR THE LOCALISATION OF THE TREATMENT VOLUME IN BREAST CARCINOMA

J. Lovett, J. A. Bullimore, E C. Whipp, P. H. Stevens, M. Halliwell, H. J. Appleby, C. S. Abbott, D. Coules and T. J. Godden

Departments of Radiotherapy and Medical Physics, Bristol Radiotherapy and Oncology Centre

Accurate delineation of the treatment volume for breast carcinoma is essential if underlying lung tissue is to be spared during the treatment of the breast tissue and contiguous nodes. To improve localisation, four different imaging modalities have been evaluated to determine the optimum method of localisation with the patient in the treatment position. The data have been collected in the following forms: (a) CT data from an EMI 5005 scanner, (b) ultrasound B-scan data from a B & K scanner with a scanning arm, (c) Cynosure 2000 CT system fitted to an Oldelft simulator and (d) conventional AP and lateral radiographs taken on the simulator.

All image data are fed into the treatment planning system, on line in the case of the CT scanner data and the Cynosure system, through a microcomputer interface for the ultrasound data or using conventional planning techniques for the outline and treatment volume determined on the simulator. For each modality, outlines or scans are taken through the same level on the patient and computer distributions produced for each level. From the information obtained, a comparison is made of the optimum imaging modality to ensure adequate radiotherapy to the treatment volume.

THE USE OF MITOXANTRONE AS A SINGLE AGENT IN THE TREATMENT OF ADVANCED BREAST CANCER

M. H Robinson, K. D Durrant and A. C. Jones

Department of Radiotherapy and Oncology, Churchill Hospital, Oxford

Early trials of Mitoxantrone have demonstrated an overall response rate of 25–30% in breast cancer. In these studies

≤ 50% patients had recieved prior hormone therapy Thirty-two consecutive patients with breast cancer, having failed hormone therapy of mean duration 20 7 months, were entered into a prospective study of the efficacy and toxicity of Mitoxantrone at a dose of 14 mg/m^2 every 3 weeks Dose escalation in 2 mg/m^2 increments was planned for those with static disease Treatment was discontinued if there was progressive disease after two courses at any dose. One patient was pre-menopausal, although seven had undergone an induced menopause Twenty-four patients had a Karnofsky status ≥ 60%. Disease was predominantly of chest wall and soft tissue (75%). Mean number of courses received was 4 (range 1–12).

Results

Evaluable (two courses)	CR	PR	SD	PD
24	1	3	10	10

Toxicity was low; no nausea with 56% of courses, diarrhoea and stomatitis negligible Of evaluable patients, 82% had no significant alopecia Neutropenia prevented dose escalation above 14 mg/m^2 in all but one suitable patient, only eight courses were delayed by it. The overall response rate using Mitoxantrone as a single agent was lower than previously reported and it needs further evaluation in the routine clinical setting.

NEW RADIOSENSITISING DRUGS

S. Dische and M. I. Saunders

Marie Curie Research Wing for Oncology, Mount Vernon Hospital, Northwood, Middlesex

In a programme to develop more effective radiosensitising drugs than misonidazole, two have emerged for clinical testing The Roche experimental drug Ro 03-8799, a lipophilic compound with a basic sidechain, has a shorter half-life in plasma than misonidazole and shows a concentration in tissues, particularly in tumour The compound developed at Stanford, SR-2508, which is a low lipophilic compound, also has a shorter half-life in plasma, and has a lower uptake in neural tissue. A prediction of the likely benefit as an hypoxic cell radiosensitiser as compared with misonidazole can be made from a knowledge of the concentration which can be achieved in the tumour cells at the time of radiotherapy. We have developed a technique of sequential administration of different sensitising drugs to the same patient, with subsequent tumour sampling so that a direct comparison of the tumour concentration can be made.

We have now completed three series of studies in which 78 tumour samples from 17 patients have been analysed. Six were given misonidazole and Ro 03-8799, eight were given SR-2508 and Ro 03-8799, and three were given all three drugs. When equal doses of the three sensitising drugs are given, both SR-2508 and Ro 03-8799 give double the concentration in tumour obtainable with misonidazole Allowing for the total permissible doses of the different drugs and their relative sensitising efficiencies, we can predict that in a 25 fraction course of radiotherapy, SR-2508 and Ro 03-8799 are likely to be five times more efficient than misonidazole in achieving radiosensitisation of hypoxic tumour cells

CHANGES IN HELPER AND SUPPRESSOR T-LYMPHOCYTES FOLLOWING RADIOTHERAPY FOR BREAST CARCINOMA

G. H. Newman, G. J. G. Rees, R. S. J. Jones, E. A. Grove and A. W. Preece

Radiotherapy and Oncology Centre, Bristol

Changes in total T-lymphocytes and two subsets in peripheral blood after radiotherapy have been followed using monoclonal antibodies Blood samples were taken from 17 women before and at intervals during the 9 months after megavoltage radiotherapy to the chest wall and axillary nodes Total white cell counts were determined in whole blood. Lymphoid cells were separated from heparinised blood by centrifugation over a density gradient Monoclonal antibodies (Beckton & Dickinson Ltd) conjugated with fluorescent markers were used to label the lymphocytes, anti-Leu 1 marking T-lymphocytes and anti-Leu 2a and 3a, respectively, defining suppressor and helper subsets At least 300 cells per sample were counted using fluorescence microscopy

Following treatment, the total lymphocyte count fell and remained significantly depressed (p < 0 02) throughout the study period, while the proportion of T-lymphocytes was unchanged Mean H . S ratios were within the normal range (1 8 to 2.2), both before and 3 months after treatment (1.90, SEM 0.2 and 1.95, SEM 0 27, respectively), but had fallen to 1.56, SEM 0 17 by 6 months and remained significantly reduced ($p < 0.02$) thereafter Thus, a fall in total T-lymphocytes with an unaltered H S ratio was followed by a recovery in cell numbers, which was greater for suppressor cells than for helper cells, with a consequent fall in H : S ratio.

PROSTATIC IODINE-125 IMPLANT UNDER ULTRASOUND GUIDANCE (A) CLINICAL CONSIDERATIONS

E. C. Whipp and H Eckert

Department of Radiotherapy, Bristol Radiotherapy and Oncology Centre

Carcinoma of the prostate is increasing in incidence, particularly in the South West of England, without apparent cause. The available treatments for localised disease include complete surgical removal of the prostate, a technique not without risk and unpleasant side-effects, and localised radiotherapy to the gland. External beam radiotherapy is effective in controlling the disease but is associated with unacceptable side-effects in 9% of cases. Brachytherapy seems to offer the advantages of control of the disease without the side-effects of radiation damage to healthy tissues. Twenty-one patients with localised prostatic cancer have been implanted with ^{125}I seeds Initially this was performed at open operation with the prostate exposed through a suprapubic incision (eight patients). The following 13 patients were implanted using a transperineal technique, the loading needles being inserted using a rectal ultrasound probe The technique and initial results are described together with proposals for improvements to the present method

PROSTATIC IODINE-125 SEED IMPLANT UNDER ULTRASOUND GUIDANCE (B) PHYSICAL PRINCIPLES

H. J. Appleby, M. Halliwell and T. J. Godden

Department of Medical Physics, Bristol Radiotherapy and Oncology Centre

Iodine 125 is an attractive radionuclide for brachytherapy. Its half-life of 60 days makes it suitable for permanent implant therapy, and as it emits low energy X rays, minimal radiation protection is required.

Iodine-125 seed implants are used to treat certain patients with early stage prostatic cancer. Seeds are implanted using needles which are inserted into the prostate through the perineum. This procedure is carried out with an ultrasound transducer located in the rectum to produce real-time images of the prostate in the transverse plane, and to show the positions of the needle tips in the gland.

Rectal ultrasound is also used prior to the implant to assess the volume and "average dimension" of the prostate and to plan the seed distribution. The average dimension is used together with a nomogram developed at the Memorial Sloan-Kettering Hospital to predict the number and activity of seeds necessary to give the required dose. Dose calculation is done by computer. The seeds are identified and their positions determined from three isocentric radiographs. The computer program then calculates and displays dose distributions in planes through the gland, and evaluates the volume of the prostate treated to particular dose levels, enabling the determination of a "matched peripheral dose" for the implant.

HYPERFRACTIONATION IN ADVANCED HEAD AND NECK CANCER: RESULTS OF A RANDOMISED CLINICAL TRIAL

V. Balasundaram, M. S. Vidyasagar and J. G. R Solomon

Department of Radiotherapy & Oncology, Kasturba Hospital, Manipal-576 119, Karnataka, India

There is no general agreement on an optimum fractionation schedule in radiotherapy, and the present practice of irradiation five times a week is based merely on administrative and economic convenience, rather than on a sound radiobiological foundation. Conventional fractionation may not be the best with respect to cellular kinetics and radiosensitivity. The radiobiological basis of hyperfractionation is discussed. The terms superfractionation and hyperfractionation are defined.

We have been treating Stage III and IV cancers of the head and neck with two and three fractions a day, over the last 3 years. We also conducted a randomised controlled clinical trial giving two fractions or three fractions a day for head and neck cancers. More than 50 cases were included in each part of the trial. This presentation reports our 3-year experience using daily multiple fractions for head and neck cancers and compares the two fractionation regimes. The skin reactions were comparable to conventional fractionation. The mucosal reactions were acceptable. The advanced head and neck cancers definitely achieved better palliation than with conventional fractionation. It would appear that there is no statistically significant difference in the results between the two fractionation regimes.

RADIOTHERAPY EMPLOYING THREE FRACTIONS EACH DAY OVER A CONTINUOUS PERIOD OF 12 DAYS

M. I. Saunders and S. Dische

Regional Centre for Radiotherapy and Oncology, Mount Vernon Hospital, Northwood, Middlesex

Radiobiological evidence now suggests that in the radiotherapy of human tumours, regrowth between fractions is much more important than was considered formerly (Fowler, 1984). Accelerated fractionation, using multiple treatments in one day, should lead to a reduction in time for regrowth between fractions. It follows, however, that with such a schedule, a pause in treatment at the week-end, or during the gap which occurs when a split course is employed, is likely to negate the benefit to be obtained.

We have administered 36 fractions of radiotherapy over a continuous period of 12 days with a 6 h gap between the first and second and between the second and third treatments on each day. Twenty patients have now been included in this Phase I study. The predicted acute reactions in the mucosa of the oral cavity and in the oesophagus were not excessive and no other immediate problems have developed. Immediate tumour responses have been remarkably promising. In five of the first seven patients with carcinoma of bronchus there has been radiological evidence of complete tumour regression, while in the remaining two, 80% regression was observed before, in one case, death due to myocardial infarct and in the other, radiation fibrosis obscured the primary site. All four patients with advanced head and neck tumours showed a rapid response in the primary site with complete regression and healing. The technique has proved to be a practical one and the promising tumour responses combined with the expectation of a low incidence of late change encourages a full exploration.

REFERENCE

FOWLER, J. F., 1984. *British Journal of Cancer, 49, Suppl. VI,* 285–300.

RADIOTHERAPY OF ADVANCED HEAD AND NECK CANCER USING MULTIPLE FRACTIONS DAILY

D. A. L. Morgan and P. J. Bradley

Departments of Radiotherapy and Otolaryngology, General and University Hospitals, Nottingham

A trial of MFD radiotherapy for advanced squamous-cell head and neck cancers was commenced in June 1983, to assess whether "radical" doses of radiation (45 Gy and over) can be delivered more rapidly than with conventional fractionation without exceeding acute normal tissue tolerance. Twenty-five patients have been treated.

Radiotherapy was given three times daily, with a minimum interval of 3 h between fractions and a fraction size of 1.1–1.5 Gy. Initially, fractions of 1.5 Gy were used, with a rest after 45 Gy in 2 weeks, followed by a "boost" to 60–70 Gy for responding tumours. Subsequently, using smaller fractions (1.1 Gy), patients with laryngeal tumours have been able to tolerate higher doses without interruption (60–65 Gy in 4 weeks). Mucosal reactions necessitated treatment interruption below 45 Gy in two frail patients, in whom a large part of the oral cavity was within the treatment volume. All other patients reached at least 45 Gy without interruption. Complete clinical responses were seen in 14 patients; two patients are as yet unassessable. In the 11 patients with laryngeal cancer, there have been no relapses at the primary site to date.

Radiotherapy using MFD, as described here, enables radical doses to be delivered quickly, particularly in laryngeal tumours, preliminary results are encouraging.

1986 Mayneord Lecture

SEEING THINGS MORE CLEARLY

G. R. Higson

Director of Scientific and Technical Services, DHSS, London

The last 20 years have seen many new developments in our ability to visualise the interior of the human body. A surprising number of these have either originated, or have had their early development stages, in the UK. The DHSS has played a part in the development and/or the introduction of several of these new devices, a role which is quite distinct from that of the normal regulatory activity of a Government department and which appears to be unique to this country. The first example of this partnership role appears to be the ultrasonic B-scanner in 1964, and it has since included all imaging modalities. The most significant has been the CT scanner introduced in 1971 but there are hopes that MRI may have a similar impact.

Besides this exciting involvement in many new developments in medical imaging, the Department has promoted a number of exercises in the measurement of performance, or some aspects of performance, of various types of medical imager, and it has put these into use either as routine quality control aids or in evaluation exercises aimed at helping radiologists make better choices of equipment.

All the work mentioned depends on close collaboration between scientists and administrators in Government, scientists and manufacturers in industry, and scientists and doctors in the NHS. Results have shown that the UK is remarkably well suited for the promotion of that collaboration

Buying for Radiology, One Day Seminar, Thursday 10th April

No abstracts published

Neuroradiology

Chairman: Dr G. Thomson

The impact of CT and MRI on imaging of the cervical spine in patients with rheumatoid arthritis, by Dr B. J. Preston, Dr R. R. Mawhinney, Dr J. H. Buckley, K. Lloyd-Jones and Professor B. S Worthington

IV DSA in intracranial aneurysms, by Dr P. Butler, Mr A. N. Jha and Mr R. H. Lye

Cranial CT findings of liver failure, by Dr J W. Lecky, Dr P. Bernthal, Dr W. E. Rothfus, Dr R. E. Teuter, Dr D. M. Van Thiel and Ms A Hays

NMR imaging in clinically isolated neurological syndromes, by Dr I. E. C. Ormerod, G. Johnson, D R. MacManus, W. I. McDonald, P. Rudge, E. P. G. H. du Boulay, B. E. Kendall and I. F. Moseley

Magnetic resonance appearances of primary intracranial lymphoma, by Dr S. McKinstry, Professor B. S Worthington, Dr P. D. Lewis and Dr J. S. Lowe

An assessment of the clinical contribution from low-field MRI in the posterior fossa, by Dr D. M. Kean, R J. Sellar, J Heath, Dr M. A Smith, Miss R. H. B. Douglas and Professor J. J. K. Best

Differential diagnosis of cerebello-pontine angle lesions by MRI, by Dr R. R. Mawhinney, Dr J. H. Buckley, Dr J. S Lowe and Professor B. S. Worthington

The corpus callosum: a reappraisal by MRI, by Professor B. S. Worthington and Dr I. M. Holland

The investigation of brain-stem gliomas using low-field MRI, by Dr D. M. Kean, Miss R. H. B. Douglas, Dr M. A. Smith and Professor J. J. K Best

MRI of periventricular leukomalacia, by Dr J. Pennock, Dr G. M. Bydder and Dr L. Dubowitz

MRI demonstration of meningeal contrast enhancement, by Dr S. McKinstry, Dr M. H. Guilleux and Dr G. M. Bydder

A case of malignant melanoma with cerebral involvement, by Dr D. M. Kean and Dr J. J. Going

A simple radionuclide technique for localising intracerebral lesions prior to neurosurgical or CT guided biopsy, by Miss J. G. Wheeler, Mr P. A. Smith, Mr R. B. Richardson and Mr H. B. Coakham

A simple technique for CT guided brain biopsy, by Dr A. J Longstaff and Mr H. B. Coakham

An assessment of the contribution of different types of MR image in the reporting of clinical MR images of the brain, by Dr D. M. Kean, Dr R. J. Sellar, Dr M. A. Smith, Miss R. H. B. Douglas and Professor J J. K. Best

THE IMPACT OF COMPUTED TOMOGRAPHY AND MAGNETIC RESONANCE IMAGING ON IMAGING OF THE CERVICAL SPINE IN PATIENTS WITH RHEUMATOID ARTHRITIS

B. J. Preston, R. Mawhinney, J. Buckley, K. Lloyd-Jones and B. S Worthington

Department of Radiology, Queen's Medical Centre, Nottingham

A study was made of 15 patients who had sufficiently severe neurological symptoms and signs and/or severe pain due to rheumatoid involvement of the neck that operative intervention was being planned. Each patient underwent plain radiography, conventional tomography, myelography, CT and MRI. Conventional tomography added little to the plain radiographs. Myelography could detect the level and extent of cord compression but assessment of the upper cervical cord with the spine in flexion was poor. Computed tomography performed shortly after myelography was found to be effective in assessing cord compression at all levels with the spine in both flexion and extension. It was also useful in showing the bony confines of the canal and atlanto-axial rotation. Magnetic resonance images of the cervical spine in the sagittal plane were of sufficient quality to detect cord compression and were able to show the effects of flexion/extension. It is concluded that magnetic resonance imaging could replace myelography for detecting cord compression If details of atlanto-axial rotation and bony outline of the spinal canal are required, then CT will provide the appropriate images.

INTRAVENOUS DIGITAL SUBTRACTION ANGIOGRAPHY IN INTRACRANIAL ANEURYSMS

P. Butler, *A. N. Jha and R. H. Lye

*Departments of Neuroradiology and *Neurosurgery, Manchester Royal Infirmary*

The limited resolution and lack of selectivity of intravenous DSA precludes its use in the pre-operative assessment of intracranial aneurysms and vascular malformations Despite this, useful peri-operative information can be obtained using the technique in such cases 3 years' experience is presented.

The presence of arterial spasm, taken in conjunction with the patients' clinical status, may influence the timing of surgery following a subarachnoid haemorrhage Examples demonstrating the utility of intravenous DSA in showing spasm affecting major intracranial vessels are given Post-operatively, the position of a surgical clip on an aneurysm can be shown and it is possible to monitor the large vascular malformations and aneurysms using intravenous DSA Conclusions are drawn with respect to the approximate size of the smallest aneurysm discernable in relation to anatomical position Consideration is given to the role of intravenous DSA in screening for aneurysms and vascular malformation in relation to CT

CRANIAL COMPUTED TOMOGRAPHIC FINDINGS OF LIVER FAILURE

J. W. Lecky, P. Bernthal, W. E. Rothfus, R. E. Teuter, D. M. Van Thiel and A. Hays

University of Pittsburgh, Pennsylvania, USA

The patient groups in this study are as follows.

(1) non-liver transplant, non-alcoholic liver failure;
(2) non-liver transplant, alcoholic cirrhotic liver failure and
(3) liver transplant with pre-transplant and post-transplant encephalopathy.

The patients were assessed as to cognitive function, intellect, learning, memory, psychomotor capacity, visual spatial capacity, attention and concentration, social functioning and emotional and psychiatric disturbances The data obtained are correlated with cranial CT findings, including assessment of atrophy and/or other cerebral parenchymal abnormalities. The cranial CT and psychological–psychiatric evaluations of these abnormal patients were then evaluated in relationship to a normal control group. The results are presented.

NUCLEAR MAGNETIC RESONANCE IMAGING IN CLINICALLY ISOLATED NEUROLOGICAL SYNDROMES

I. E. C. Ormerod, G. Johnson, D. R. MacManus, W. I. McDonald, P. Rudge, E. P. G. H. du Boulay, B. E. Kendall and I. F. Moseley

The National Hospital for Nervous Diseases, London

The sensitivity of nuclear magnetic resonance imaging (NMRI) in demonstrating abnormalities within the brain in multiple sclerosis (MS) is well established We, therefore, used a 0.5 T Picker NMRI system, imaging protons to study a group of patients with clinically isolated neurological syndromes of a type known to be common in MS. These were patients in their first neurological episode with no previous history. Thirty-eight patients with optic neuritis, 30 patients with clinically isolated brain-stem syndromes and 30 patients with isolated syndromes of the spinal cord were examined. Clinically unsuspected disseminated lesions within the brain were seen in 62%, 74% and 53% of patients, respectively.

Nuclear magnetic resonance imaging was more sensitive than evoked potentials in demonstrating the presence of disseminated lesions; it was also more sensitive than evoked potentials in demonstrating the presence of abnormalities which might be responsible for the presenting brain-stem and spinal-cord syndromes. However, visual evoked potentials were more sensitive than NMRI in detecting abnormalities within the optic nerve in patients with optic neuritis. From a study of acute and chronic lesions of the brain stem, measurements of the T_1 and T_2 characteristics of individual lesions may allow an estimate to be made of their age The prognostic significance for patients with NMRI abnormalities at presentation is not yet established.

MAGNETIC RESONANCE APPEARANCES OF PRIMARY INTRACRANIAL LYMPHOMA

S. McKinstry, B. S. Worthington, P. D. Lewis and J. S. Lowe

Department of Diagnostic Radiology, Royal Postgraduate Medical School, Hammersmith Hospital, London

The NMR appearances of primary intracranial lymphoma have not been described previously. Four histologically proven cases are discussed and comparison is made with the findings on CT The difficulties in diagnosing this rare but radiosensitive tumour are discussed.

The material comprises three female and one male patient aged from 10 to 61 years. All presented with neurological symptoms and none had evidence of systemic disease The NMR scans used a variety of spin echo and inversion recovery sequences Computed tomography consistently showed less extensive changes than NMR; contrast enhancement was seen in two cases Nuclear magnetic resonance demonstrated multiple lesions in all cases and all showed periventricular involvement. Mass effects were not prominent. One case was given intravenous gadolinium-DTPA and enhancement was seen.

Primary intracranial lymphoma tends to involve deep, central structures with subependymal periventricular spread. There is a high incidence (30–45%) of multifocal disease On CT the lesions are often confused with other tumours and metastases The increased sensitivity of MR leads to increased detection of multifocal disease; however, the periventricular distribution and lack of mass effect may be confused with white-matter disease.

AN ASSESSMENT OF THE CLINICAL CONTRIBUTION FROM LOW-FIELD MAGNETIC RESONANCE IMAGING IN THE POSTERIOR FOSSA

D. M. Kean, R. J. Sellar, J. Heath, M A. Smith, R. H B. Douglas and J. J. K. Best

NMR Imaging Unit, University of Edinburgh, Royal Infirmary of Edinburgh

An attempt has been made to assess the clinical contribution to the diagnosis and management of patients from the use of MRI in the investigation of the posterior fossa One hundred patients with a variety of neurological and neurosurgical problems were examined and the MR examination compared with other investigations (in most cases CT). The results of all tests were analysed along with the patients' clinical notes A neurological and neurosurgical opinion was also obtained as to the contribution MRI had made in each case. In all cases where the examinations were abnormal, MRI was considered to be superior and made the abnormality more conspicuous. In all cases of suspected pathology at the craniovertebral junction, MRI was considered to be superior and should now be considered to be the imaging technique of first choice Deficiencies of MRI included some lack of specificity where contrast-enhanced CT was superior, the lack of calcium demonstration, and the inability to image in the vicinity of even small amounts of metal.

DIFFERENTIAL DIAGNOSIS OF CEREBELLO-PONTINE ANGLE LESIONS BY MAGNETIC RESONANCE IMAGING

R. R. Mawhinney, J. Buckley, J. S Lowe and B. S Worthington

Department of Human Morphology, University of Nottingham

The MRI features of 20 assorted lesions occurring at the cerebello-pontine angle are examined. These constitute 16 tumours, all proven histologically, and four vascular lesions Differences in spin sequence characteristics were found between neurilemmomas (nine lesions) and meningiomas (five lesions) with neurilemmomas typically exhibiting a greater increase in T_2 than meningiomas While T_1 images were of less value in differentiation between neurilemmomas and meningiomas, they were of great value in the diagnosis of vascular lesions due to the decreased T_1 of blood clot. T_1 images were also of help in assessment of tumour size

Extension of tumour into the internal auditory meatus (IAM) was demonstrated on all but one of the acoustic neuromas in which IAM widening was present on CT. With the exception of a congenital cholesteatoma, it was not found with any of the other lesions The transverse perspective was of the greatest value in lesion assessment, though the coronal perspective may be of value with large lesions. The sagittal perspective is generally of little help

The neurilemmomas were examined for any possible correlation between spin sequence characteristics and histological features but none could be shown. Similarly, no correlation was found between spin characteristics and surgical findings of tumour consistency.

THE CORPUS CALLOSUM: A REAPPRAISAL BY MAGNETIC RESONANCE IMAGING

B. S. Worthington and I. M. Holland

Department of Academic Radiology, Queen's Medical Centre, Nottingham

The advent of MRI has provided a direct sagittal and coronal perspective in sectional brain imaging and this, together with the excellent discrimination between grey and white matter, facilitates the study of the corpus callosum with an unparalleled clarity. Because of its relatively firm consistency it was called "the hard body" by early anatomists, but MR studies show it to have a remarkable pliability able to tolerate stretching and thinning in hydrocephalus and a range of deformities when compressed by adjacent mass lesions. It has, however, only a limited capacity to regain its original configuration when the source of deformity is removed. Congenital abnormalities, such as agenesis or lipoma, are elegantly assessed and vascular malformations can be shown without the need for contrast medium injection Areas of demyelination and shearing injuries which are not apparent on CT can now be shown. Primary tumours of the corpus callosum can be detected before there is any significant alteration in the size or morphology and secondary involvement by hemisphere tumours with transcallosal spread can be detected with a sensitivity exceeding that of CT. The information gained from MRI studies has facilitated the transcallosal approach to tumours such as intraventricular ependymomas.

THE INVESTIGATION OF BRAIN-STEM GLIOMAS USING LOW-FIELD MAGNETIC RESONANCE IMAGING

D. M. Kean, R. J. Sellar, R. H. B. Douglas, M. A. Smith and J. J. K. Best

NMR Imaging Unit, University of Edinburgh, Royal Infirmary of Edinburgh

The identification of brain-stem gliomas can be difficult using conventional methods such as X-ray CT; this may have tragic consequences since most of these tumours occur in a younger age group A low-field (0.08 T) MRI system installed in the Royal Infirmary of Edinburgh has detected several examples of brain-stem glioma and these demonstrate the advantages of MRI in the investigation of this type of pathology In two cases the prolongation of relaxation times allowed the identification of a lesion to be made when a CT examination was negative. In all cases the sagittal and coronal planes available in MRI provided very precise localisation of the tumour In one case haemorrhage into a tumour was identified on MRI, and in all cases decrease in both the size and relaxation times was clearly seen after therapy.

MAGNETIC RESONANCE IMAGING OF PERIVENTRICULAR LEUKOMALACIA

J. Pennock, G. Bydder and L. Dubowitz

Departments of Radiology and Neonatal Medicine, Royal Postgraduate Medical School, Hammersmith Hospital, London

The purpose of this study was to observe the development of myelination and appearance of periventricular leukomalacia (PVL) and subcortical leukomalacia (SL) with age using MRI. The diagnosis of PVL (five infants) and SL (two infants) was made by ultrasound The examinations were done in a 0 15 T Picker prototype machine. High-resolution, age-adjusted inversion-recovery scans were used to assess myelination and the distribution of the leukomalacia Transverse scans were obtained through the ventricles and the centrum semiovale.

The children with PVL showed an increase in white matter at each examination. In early life, leukomalacia was best seen in the centrum semiovale as clearly defined areas of long T_1. The cysts shrank in size but were still evident at 18 months. At mid-ventricular level the posterior horns were enlarged with a characteristic irregular outline suggestive of cyst coalescence. No myelin was identified in one infant with SL examined at 38 weeks and 5 months, however, there was shrinkage of the extensive cysts with an increase in ventricular size The second child, examined at 8 months, had myelin in the internal capsule and multiple large cysts around the ventricles No change was seen at 18 months of age

MAGNETIC RESONANCE IMAGING DEMONSTRATION OF MENINGEAL CONTRAST ENHANCEMENT

S. McKinstry, M. H. Guilleux and G M Bydder

Department of Radiology, Hammersmith Hospital, London

The absence of artefact or partial-volume effect from cortical bone enables the region of the meninges to be seen clearly with MRI. Seventy-three cases in which MRI examinations were performed following administration of intravenous gadolinium-DTPA were reviewed in order to determine the clinical situations in which meningeal enhancement may be seen.

Evidence of enhancement was seen in cases of meningioma, astrocytoma, sarcoidosis and subdural haematoma and following surgical resection Histological correlation in cases of meningioma displayed dural extension in one case and reactive change in a second case. The membrane surrounding subdural haematoma enhanced both medially and laterally.

While dural enhancement may occasionally be seen with CT particularly following removal of a bone flap, meningeal enhancement appears more common with MRI and may be of value in detecting tumour infiltration as well as infective and non-infective forms of meningitis.

A CASE OF MALIGNANT MELANOMA WITH CEREBRAL INVOLVEMENT

D. M. Kean, M. A. Smith, R. H. B. Douglas, J. J. Going and J. J. K. Best

NMR Imaging Unit and Department of Pathology, University of Edinburgh, Royal Infirmary of Edinburgh

The CT scan of a 60-year-old man was performed and was reported as showing possible abnormalities in the frontal regions, and so an MR examination was performed A sagittal T_1 image showed a mass lesion in the sphenoid sinus. The T_1 of this mass was close to that of grey matter (340 ms at 0.08 T) Several other lesions were also seen in both frontal areas It was noted that as well as having longer relaxation times relative to the primary site (sphenoid), the cerebral lesions also show varying relaxation times relative to one another. Unfortunately the patient deteriorated and soon died. The brain slices demonstrated the typical appearances of widespread melanoma The sections through the brain stem show a large deposit which was only identified in retrospect. This case demonstrates that some tumours have "short" relaxation times, that the relaxation times and, therefore, the MR appearances of the same tumour type can display wide variations, and that great care must be taken when analysing NMR images since some malignancies such as melanoma may have short relaxation times and be difficult to identify

A SIMPLE RADIONUCLIDE TECHNIQUE FOR LOCALISING INTRACEREBRAL LESIONS PRIOR TO NEUROSURGICAL OR COMPUTED TOMOGRAPHY GUIDED BIOPSY

J. G. Wheeler, P. A. Smith, *R. B. Richardson and †H. B. Coakham

*Department of Nuclear Medicine, *Department of Medical Physics, and †Department of Neurosurgery, Frenchay Hospital, Bristol*

After a suspected intracerebral lesion has been confirmed by CT scanning, it may be necessary to assess its histology prior to treatment using tissue samples obtained by burr-hole biopsy (BHB) or craniotomy Precise prior location of lesions gives a high success rate in obtaining diagnostic tissue samples. Previous localisation techniques had certain disadvantages, often due to complexity We have developed a simple, accurate method using the radionuclide ^{99}Tc^{m}. The patient is positioned under a gamma camera so that a true lateral view of the affected side of the head is obtained. The resultant image is viewed on a persistence scope and a ^{57}Co marker-pen used as a visual aid to locating the lesion. A small lead disc is taped to the patient's scalp at a site corresponding to the lesion's centre After accumulating hard-copy data with the disc *in situ*, it is removed and replaced by an indelible mark on the skin surface This is later used as a precise guide for BHB or placement of small craniotomy Two hundred patients have undergone this straightforward localisation technique, which has increased the operative success rate at first attempt from 88% overall (82% BHB) to around 95% (93% BHB).

A SIMPLE TECHNIQUE FOR COMPUTED TOMOGRAPHY-GUIDED BRAIN BIOPSY

A. J. Longstaff and *H. B. Coakham

*Departments of Radiology and *Neurosurgery, Frenchay Hospital, Bristol BS16 1LE*

Computed tomography is well established as a technique for needle guidance in percutaneous biopsy of lesions in many organs, particularly in the abdomen. We have evolved a simple technique for needle placement within the brain, for biopsy and cyst drainage Both techniques require either burr-hole or craniotomy for access through the skull vault. The latter situation will pertain in the post-operative patient, but the majority of subjects will require a burr hole, the site for which can easily be established using the technique described by Wheeler et al (this meeting) A scan is obtained through the "window" in the skull vault and the required depth and angle of needle penetration established using the software facilities on the scanner.

The needle, or catheter over needle assembly, is then introduced and the tip position checked by a repeat scan The problem of artefact caused by the metallic needle can be overcome by using a plastic sheath, from which the stiffening stilette or needle can be withdrawn before the check scan is made. The biopsy needle may then be re-inserted down the sheath for sampling or aspiration. This can usually be done in the scanning room, but if the patient is required to go to theatre, the plastic sheath can be folded down at the skin surface and taped securely during transit

This simple and rapid technique, which does not require complex and expensive stereotactic devices, has been used effectively and safely in biopsy and cyst drainage Examples are given

AN ASSESSMENT OF THE CONTRIBUTION OF DIFFERENT TYPES OF MAGNETIC RESONANCE IMAGE IN THE REPORTING OF CLINICAL MAGNETIC RESONANCE IMAGES OF THE BRAIN

D. M Kean, R. J. Sellar, M. A. Smith, R. H. B. Douglas and J. J. K. Best

NMR Imaging Unit, University of Edinburgh, Royal Infirmary of Edinburgh

Magnetic resonance images are influenced by several factors such as T_1, T_2, proton density and flow. These factors alter signal intensity as does the pulse sequence used The final MR image can sometimes be difficult to interpret, particularly for an inexperienced operator. One solution to this problem may be to employ a "standard" pulse sequence such as the interlaced saturation-recovery/inversion-recovery employed on a low-field (0 08 T) system which has been installed in the Royal Infirmary of Edinburgh. The four different types of image available on this system have been "scored" in the course of an MR/CT comparison and it has been shown that the calculated T_1 image was the most useful image in making clinical diagnoses The proton density image had the best spatial resolution of the available images but provided less pathological information than the others However, it was useful in defining normal anatomy and showing areas of both short and long T_1.

Bone Radiology

Chairman: Dr Myles McNulty

The application of photon densitometry to fracture healing, by Mr P. E. Watkins, D. J. Kelly, J A. Leendertz, H. S. Rigby and A E. Goodship

Effects of variation in the size of the region of interest on the accuracy of CT bone densitometry, by Dr J E. Adams, Mr J. B. Carter and Professor P. H. Adams

Comparison between body calcium, hand- and spine-bone mineral in patients with asthma or rheumatic disease, by Dr P. Tothill, Dr J J. Nicoll, Dr D. W. Pye, Dr E. Law, Dr M. A. Smith, Dr Reid and G. Nuki

THE APPLICATION OF PHOTON DENSITOMETRY TO FRACTURE HEALING

P. E Watkins, D. J. Kelly, J A. Leendertz, H. S Rigby and A. E. Goodship

Department of Anatomy, School of Veterinary Science, University of Bristol

A technique of dual source photon densitometry using ^{125}I and ^{241}Am has been developed for the assessment of bone mineral content at the site of healing of experimental fractures The experimental model is a mid-diaphyseal osteotomy of the sheep's tibia stabilised by use of an external fixation device. This allows accurate positioning and subsequent relocation of the fracture at the time of scanning Sequential scans are performed at regular intervals over a period of 12 weeks, and at each examination multiple scans are performed in two planes at the fracture site. There is a statistically significant correlation (at 5%, Spearman rank correlation coefficient) between bone mineral content at the healing fracture and post-mortem torsional strength The technique of photon densitometry has also been applied to the diagnosis and monitoring of experimental oligotrophic non-union fractures in two species. Photon absorption densitometry has been demonstrated to be a useful non-invasive technique for the assessment of bone mineral content at the site of healing fractures. Its application to clinical orthopaedics remains limited both by the geometry of clinical fractures and by the methods of treatment currently in use, few of which would facilitate application of this technique

EFFECTS OF VARIATION IN THE SIZE OF THE REGION OF INTEREST ON THE ACCURACY OF COMPUTED TOMOGRAPHIC BONE DENSITOMETRY

J. E. Adams, *J. B. Carter and †P. H. Adams

*Departments of Diagnostic Radiology, *Medical Biophysics and †Medicine, University of Manchester*

Various sizes and shapes of the region of interest have been used in studies of bone mineral measurement using quantitative CT. We have examined the influence of different sizes of the region of interest on the accuracy of CT measurement of trabecular bone mass in sites in the proximal and distal femur and in the lumbar spine. Cadaver lumbar vertebral bodies and femora were scanned on a GE 8800 CT scanner using a single-energy technique. Computed tomography attenuation values were obtained for a central region of interest and the total trabecular bone area. The section scanned was excised and the composition of the regions of interest measured by chemical analysis.

The chemical composition and CT attenuation of the central regions were strongly correlated with those of the total areas from which they were derived The values for the central region were lower than those of the whole trabecular bone space. In the vertebrae there was a significant relation between mineral concentration and CT attenuation of the central area; no significant difference was found between the means of the predicted and measured mineral content at this site The mean predicted mineral concentrations of the total vertebral areas, and of the central and total areas of the femoral samples were all significantly less than those measured by chemical analysis. A small central region of interest provides the more accurate estimate of vertebral trabecular bone mass. A group of 42 patients with miscellaneous metabolic bone disorders was examined, and similar significant relations were found between CT attenuation values of a central region of interest and the total trabecular bone space.

COMPARISON BETWEEN TOTAL BODY CALCIUM, HAND- AND SPINE-BONE MINERAL IN PATIENTS WITH ASTHMA OR RHEUMATIC DISEASE

P. Tothill, J. J. Nicoll, D. W. Pye, E Law, M. A. Smith, D Reid and G. Nuki

Departments of Medical Physics and Rheumatology, University of Edinburgh

Total body calcium was measured by *in vivo* neutron activation analysis, hand-bone mineral by single photon absorptiometry, and spine-bone mineral by dual photon absorptiometry in groups of patients with asthma or a variety of rheumatic diseases, some of whom had been treated with corticosteroids. Results were compared with those predicted by equations derived by regression analysis from measurements on normal subjects, taking into account sex, age and body size. As expected, the three measurements correlated well when unnormalised results were used. Correlation was much worse when the results were expressed as per cent of normal. It is not surprising that bone loss consequent upon disease or treatment with corticosteroids may not be uniform throughout the skeleton The results throw light on the relative magnitude of appendicular, axial and whole-body bone mineral deficits in several diseases

MRI Physics

Chairman: Dr P. C. Jackson

The installation of a high-field NMR system for spectroscopy and imaging, by Dr M. O. Leach

A comparison of signal-to-noise levels from several receiver coil designs in NMR imaging, by Dr R. A. Lerski, Mr D. W. McRobbie, Mr K. Straughan, Mr S. Jennings and J. S. Orr

Effect of electrical field coupling as a limit on close-coupled coils, by M. Burl, I. R. Young, A. S. Hall and P. C. Butson.

A dual-frequency NMR surface coil for proton imaging and ^{31}P spectroscopy, by Dr M. O. Leach, A. Hind, R. Sauter, H. Requardt and H. Weber, Sutton

Imaging and integrity of the 2-D slice in MRI, by Dr D. W. McRobbie, Dr R. A. Lerski, Dr K. Straughan, Dr P. Quilter, R. J. Willetts and J. S. Orr

T_1 measurements from images either through recording the full relaxation curve or from simple two-point techniques, by Mr K. Straughan, Mr P. M. Walker, Dr R. A. Lerski and Professor J. S Orr

Precision in the measurement of relaxation times from the minimum number of NMR images, by Dr G. Johnson, Dr I. E. C. Ormerod, Dr P. S. Tofts, Mr D. MacManus and Dr D. Barnes

Flow measurement using field echoes, by Dr J. A. Payne, I. R. Young, S. Khenia and Dr G. M. Bydder

A technique for velocity imaging using MRI, by Mr J. P. Ridgway and Dr M. A. Smith

Assessment of image quality in MRI, by Dr A. Todd-Pokropek, L Gordon and R. Jaszczak

THE INSTALLATION OF A HIGH-FIELD NUCLEAR MAGNETIC RESONANCE SYSTEM FOR SPECTROSCOPY AND IMAGING

M. O. Leach

Department of Physics, Institute of Cancer Research and The Royal Marsden Hospital, Sutton, Surrey

A 2 T Magnetom NMR system has been installed at the Royal Marsden Hospital at Sutton, for research into the applications of NMR in oncology. The installation of a high-field system on a hospital site has presented a variety of problems, particularly in terms of ensuring that the environment does not affect the homogeneity of the magnetic field and that the magnet does not affect neighbouring imaging and treatment equipment. Particular care has had to be taken in the location of structural steelwork and in avoiding mobile steel objects within the building Other important considerations are the safety of patients and staff and the emergency services. The magnet has been housed in a new building, much of which is free of steel. The magnet is enclosed in an RF screened room and provision is made to vent externally any gases released should the magnet quench. Initially, the magnet is expected to operate at a field strength of 1.5 T

A COMPARISON OF SIGNAL-TO-NOISE LEVELS FROM SEVERAL RECEIVER COIL DESIGNS IN NUCLEAR MAGNETIC RESONANCE IMAGING

R A. Lerski, D. W. McRobbie, K. Straughan, S Jennings and J S. Orr

Department of Medical Physics, Royal Postgraduate Medical School, Hammersmith Hospital, London

The importance of optimising signal-to-noise levels in NMR imaging is well recognised and, at least in the USA, it has become common to increase the static field to obtain an improved intrinsic signal-to-noise level. However, with low-field systems it is possible to make substantial gains through careful attention to coil design and matching to the pre-amplifier. The present study used the method of Edelstein et al (1984) to investigate quantitatively the fundamental signal-to-noise levels obtainable from different coil designs and with matching adjustment It has been confirmed that low-field resistive systems can compare favourably with medium-field superconducting systems if special coils and matching are utilised.

REFERENCE

EDELSTEIN, W A, BOTTOMLEY, P. A & PFEIFER, L M, 1984. *Medical Physics, 11*, 180–185.

EFFECT OF ELECTRICAL FIELD COUPLING AS A LIMIT ON CLOSE-COUPLED COILS

M. Burl, *I. R. Young, *A. S. Hall and *P. C. Butson

*NMR Unit, Hammersmith Hospital, London and *GEC Hirst Research Centre, Wembley, Middlesex*

The general gain to be obtained from the use of tightly coupled receiver coils in NMR imaging has been reported now by a number of groups, with a perception that they can offset the gain in signal-to-noise ratio with field, to a substantial degree. The degree of closeness of coupling which is possible is crucial, since the filling factor (or ratio of the volume of the voxel to the effective volume of the coil) appears as a linear variable on the signal-to-noise ratio equation It is primarily limited by the electrical coupling between coil and body.

The paper reviews the theory of the coupling using a simplified but adequate model, and notes the dependence of the capacitive loading on field (which means that coupling has to be less tight at higher fields) Practical results are presented which indicate the general utility of the model. As a result, it is possible, in conjunction with a recently developed model for the inductive coupling between coil and body, to reach a view as to the layout of efficient coils when the extra criterion of field homogeneity is also introduced.

A DUAL-FREQUENCY NUCLEAR MAGNETIC RESONANCE SURFACE COIL FOR PROTON IMAGING AND ^{31}P SPECTROSCOPY

M. O. Leach, *A. Hind, †R. Sauter, †H. Requardt and †H. Weber

*Department of Physics, Institute of Cancer Research and Royal Marsden Hospital, Sutton, Surrey, *Siemens Ltd, Sunbury-on-Thames, Surrey and †Siemens UB-Med, Erlangen, FRG*

A dual-frequency surface coil has been developed to enable accurate localisation of small lesions prior to ^{31}P spectroscopy by measuring both a proton image and a phosphorus spectrum with the same coil The coil makes use of simulated quarter-wavelength transmission lines to ensure that the performance of the coil at one frequency is not adversely affected by the tuning circuitry for the other frequency The unloaded Q of the coil is about 200 at 63 MHz and 26 MHz and, when loaded, the coil Q is 90 at 63 MHz and 140 at 26 MHz It is proposed that the coil be used in conjunction with methods of restricting the sensitive volume for spectroscopy and may also be used to allow the spatial sensitivity of spectroscopic studies to be quantified. The design of the coil is discussed and initial images and ^{31}P spectra are presented.

IMAGING AND INTEGRITY OF THE TWO-DIMENSIONAL SLICE IN MAGNETIC RESONANCE IMAGING

D. W McRobbie, R. A. Lerski, K. Straughan, P Quilter, R J. Willetts and J. S. Orr

Department of Medical Physics, Royal Postgraduate Medical School, Hammersmith Hospital, London

Integrity of the 2D slice is important in MRI because the characteristics of the slice strongly affect other performance features, namely, signal-to-noise ratio, spatial resolution and relaxation time contrast and measurement accuracy

Assuming a Gaussian RF amplitude modulation, the slice profile has been calculated in the steady-state condition for various sample T_1 values for saturation recovery (SR) sequences. Experimental measurements were made on a 0.1 T 60 cm-bore, resistive, purpose-built imaging system using a scanning sequence with a slice-select gradient (z) and a phase-encoding gradient, with the rephase portion of the select gradient used for readout The 2D FFT of the collected echo data was used to form a 2D projection image of the slice in whichever direction the phase-encoding gradient was applied.

There was qualitative agreement between theory and experiment, although quantitative comparison was less satisfactory. Acknowledgment is made for the support of the DHSS and the encouragement of J. L Williams

T_1 MEASUREMENTS FROM IMAGES EITHER THROUGH RECORDING THE FULL RELAXATION CURVE OR FROM SIMPLE TWO-POINT TECHNIQUES

K. Straughan, P. M. Walker, R. A. Lerski and J. S. Orr

Department of Medical Physics, Royal Postgraduate Medical School, Hammersmith Hospital, London

In clinical NMR imaging there is great interest in the use of quantitative T_1 and T_2 values for tissue characterisation However, there is still considerable doubt about the most appropriate method of carrying out the measurements, given the constraint of limited imaging time in clinical practice

The present study was designed to compare T_1 values obtained from a bench-top NMR spectrometer and an NMR scanner. In the latter case, two methods were used: a simple two-point technique of the type often used in commercial equipment and a multi-tau inversion recovery method. Test materials used were doped agarose gels with T_1 values from 66 ms to 488 ms. All scanning was performed at 0.1 T on the Medical Physics Department's resistive scanner. For the multi-tau inversion recovery data a three-parameter exponential fitting program was used. In all cases the multiple tau measurements were superior to those derived from the two-point data, which were only satisfactory over a rather limited T_1 range.

Acknowledgement is made for the support of the DHSS and the encouragement of J. L. Williams

PRECISION IN THE MEASUREMENT OF RELAXATION TIMES FROM THE MINIMUM NUMBER OF NUCLEAR MAGNETIC RESONANCE IMAGES

G. Johnson, I. E. C Ormerod, P. S. Tofts, D. MacManus and D. Barnes

The National Hospital for Nervous Diseases, London

If NMR relaxation time data are to yield useful pathological information it is more important that the measurements should be precise (*i e.* lacking random error) than accurate (*i e* lacking systematic error). The precision of a measurement determines its value in differentiating between different states. It is important to distinguish between the imprecision inherent in a measurement and real variations in the measured value. We have investigated the imprecision of relaxation times derived from the minimum number of images necessary for the calculation (three) Measurements were made on phantoms and the brains of normal control subjects and patients examined in parallel and serial studies. Scans were performed on a 0 5 T Picker imager. All scans were multislice, so a 10 cm block of tissue could be examined in 30 min The standard deviation of brain tissue measurements was 7% for T_1 and 12% for T_2. This precision was sufficient to reveal a significant difference between the relaxation times of brain tissue in different locations, although this may be due to spatial variations in imager response of differences in partial volume effects. There was also a significant difference between white matter in normal controls and apparently unaffected white matter in multiple sclerosis patients

FLOW MEASUREMENT USING FIELD ECHOES

J. A Payne, I. R. Young, S. Khenia and *G. M. Bydder

*Hirst Research Centre, GEC Research Limited, Wembley, Middlesex; *NMR Unit, Hammersmith Hospital, London*

Several groups have published work describing the measurement of the velocity of flowing material by determining the phase differences observed when images with and without the appropriate gradient pulses are compared Other workers have attempted to derive flow results from amplitude measurements, or "time of flight" methods. Generally, these have been unsatisfactory since the accuracy of formation of slices is difficult to control We describe methods using field echoes to obtain phase encoding for flow (and having both magnitude and directional sensitivity). In the first method two images are compared for phase, the difference between them being in the relative timing of the slice selection rephasing pulses Because the rephase pulse is very large, the time shift needed to give a full-scale range of a few tens of millimetres per second is small. A variant of the technique can be used for in-plane flow. an approach similar to a method described recently by the Massachusetts General Hospital group. The method involves unbalancing the timing of data acquisition and echo formation in the field-echo sequence and results in an image with characteristic phase shapes across it. The two techniques can be used, with some difficulty in interpretation, at the same time, to give flow in two directions at once Clinical examples are given of the use of the methods.

A TECHNIQUE FOR VELOCITY IMAGING USING MAGNETIC RESONANCE IMAGING

J. P. Ridgway and M. A. Smith

NMR Imaging Unit, University of Edinburgh, Royal Infirmary of Edinburgh

Much work has already been done on the effects of flowing blood and movement in MRI In addition, techniques have been developed in order to try and quantify velocities of flowing blood using phase information Many of these techniques are, however, limited, firstly by main field and gradient field non-uniformities and secondly by signal losses from flowing blood In our technique, field non-uniformities are overcome by subtracting two sets of phase information with different velocity encoding This velocity encoding is acheived by altering the time at which the rephase pulse of the slice selection gradient occurs. A field echo rather than a spin echo is used and so spin washout is not a significant cause of signal loss. As a result, high velocities perpendicular to the slice can be imaged Images have been obtained from flow phantom studies, volunteers and patients demonstrating high-velocity flow perpendicular to the imaging slice in the range 1–120 cm s^{-1}. Good correlation was found with Doppler ultrasound measurements.

ASSESSMENT OF IMAGE QUALITY IN MAGNETIC RESONANCE IMAGING

A. Todd-Pokropek, *I. Gordon and †R. Jaszczak

*University College London, *Hospital for Sick Children, London and †Duke University, North Carolina, USA*

Image quality in MRI is not only important, but very difficult to assess A phantom designed for this purpose has been tested and results obtained on nine different MRI systems, ranging in field strength from 0.5 to 1.5 T The phantom comprises five main sections, which may be imaged simultaneously The resolution insert demonstrated considerable variations as a function of position. The slice-thickness insert enabled the slice profile to be measured at various positions The spatial-distortion insert gave little useful information. A set of bottles could be filled with various concentrations of doped water, and showed considerable variations in the accuracy of T_1 and T_2 estimation, compared with theoretical predictions. A uniform section enabled magnetic and RF uniformity to be assessed, with occasionally alarming results. Testing of systems using multi-echo and/or multi-slice pulse sequences sometimes indicated problems not apparent with single echo/slice acquisitions Intercomparison of results of systems from different manufacturers may be misleading. However, the use of this phantom has brought to light problems, usually associated with the "fine adjustment" of the system, which resulted in a loss of image quality in certain acquisition modes which otherwise were not readily apparent. A detailed imaging protocol for use with such a phantom is proposed

Image Management

Chairman: Dr C. J. Taylor

Processing of CT data to remove artefacts associated with surgical clips, by Dr R. Norbury and D. Nicholas
Investigation of applicability of digital processing to ultrasound images, by Dr T. K. Hames, K. N. Humphries and M Nixon
Miniaturisation 4 years on—the results of trials, practical project studies and the full application, by C. Redman
Measurements of contrast detail detectability and information capacity of CT scanners, by Dr K Faulkner and Dr B. M. Moores
Mammography and computer-assisted diagnosis, by Dr A G. Gale, E. J. Roebuck and Professor B. S. Worthington
Automatic evaluation of dynamic radionuclide studies using principal components analysis, by Dr K. S. Nijran and Dr D. C. Barber
Utility of the early acquisition of data, by Dr I. R. Young, J. A. Payne, S. Khenia and G. M. Bydder
Modality interface and networking, by Mr R. Bader
Data storage efficiency and information redundancy in digital images. An analysis and practical approach to improvements for clinical sites in CT, by Dr C. J. Moore
A system for the production of flexible film image formats from a computer display, by Mr C. P. Wells and Dr P. J. Mountford
A new display technique for CT scans based on histogram equalisation, by Mr P. F. Wankling and Dr J A. Newell
3-D CT reformations in the assessment of congenital craniofacial anomalies, by Dr J. E. Gillespie, Professor I. Isherwood, Dr G. Barker, Dr C. Bannister and J. Lendrum

PROCESSING OF COMPUTED TOMOGRAPHIC DATA TO REMOVE ARTEFACTS ASSOCIATED WITH SURGICAL CLIPS

R. Norbury and D Nicholas

Royal Marsden Hospital, Sutton, Surrey

Patients who undergo surgery for the excision of cancerous lesions are often referred for appraisal of later tumour regrowth As these patients usually present with metallic surgical clips inserted at the operation site, severe problems are caused when CT examinations are performed Conventional reconstruction techniques cannot adequately cope with the high electron density of these clips in comparison with the density of surrounding tissue. Furthermore, any slight movement of the clips during the scanning process results in "streak" artefacts on the resulting image The existence of these artefacts in the reconstructed image restricts appraisal of the site of interest and in many instances prevents the diagnostician from viewing the surgical site at all Techniques for processing the original CT data prior to reconstruction are discussed and methods suggested which, in many instances, can remove or reduce to an acceptable level these unwanted "artefacts".

Proceedings of The British Institute of Radiology

INVESTIGATION OF APPLICABILITY OF DIGITAL PROCESSING TO ULTRASOUND IMAGES

T. K. Hames, K. N. Humphries and *M. Nixon

*Department of Medical Physics, Southampton General Hospital and *Department of Electronics and Information Engineering, University of Southampton*

The concept of multimodality digital image presentation of patient data is finding increasing clinical acceptance and encourages investigation of further processing of the information in an attempt to achieve improved extraction and display of the significant diagnostic features of the examination. The optimum processing will invariably differ for each modality.

In duplex scanning of the peripheral circulation, the diagnostic information is a combination of real-time B-mode and Doppler ultrasound. High quality non-invasive scans indicating areas of abnormality (*e.g.* early arterial disease), comparable in accuracy to conventional X-ray techniques are available. Some processing, *e.g.* compression of the data, is available on most equipment, but more sophisticated techniques such as edge detection, histogram equalisation and contrast enhancement are presently being assessed off-line. Real-time B-scan images were obtained with a Honeywell Ultraimager duplex scanner using a probe operating frequency of 5 MHz. A videodigitiser capable of 128 pixel × 128 pixel by 8-bit depth conversion was utilised and these images were processed using the SAIDIE image processing package which runs on a DEC PDP 11/23 microcomputer.

The pilot study suggests that ordered manipulation of digitised images is feasible and is a potentially useful technique. Additional areas of use could include improvement in plaque typing and ulcer detection by ultrasound, in addition to multimodality overlaying of images for quantitative and longitudinal comparison.

MINIATURISATION 4 YEARS ON: THE RESULTS OF TRIALS, PRACTICAL PROJECT STUDIES, AND THE FULL APPLICATION

C. Redman

MISS Imaging, London

The paper traces the development of the miniaturisation of archival radiographs and discusses new technology and equipment teething troubles. Impact throughout all levels of the hospital, not just the radiology department, is considered, along with quality control, in house or bureau, the role of the DHSS, cost and value, and ethical considerations. Interface with development communication systems is covered. The paper concludes by recommending a general implementation policy.

MEASUREMENTS OF CONTRAST DETAIL DETECTABILITY AND INFORMATION CAPACITY OF COMPUTED TOMOGRAPHY SCANNERS

K. Faulkner and B. M. Moores

Physics Department, Christie Hospital and Holt Radium Institute, Manchester

A range of contrast detail detectability phantoms has been designed to assess the imaging performance of CT scanners. Measurements have been made on a number of different machines and the results are presented. The imaging performance of both the image reconstruction and post-processing filters has been investigated on one particular scanner. Measurements were also made to look at the energy dependence and the effect of additional filtration on contrast detail detectability.

It is possible to deduce the information capacity of CT scans from the contrast detail detectability curves. Results of these calculations from a number of CT scanners are presented. The information capacities of CT scanners are compared with other imaging systems such as film/screen combinations, image intensifiers and direct viewing fluoroscopy. Both contrast detail detectability and information capacity curves have a useful role in comparing the imaging performance of CT scanners and other imaging systems.

MAMMOGRAPHY AND COMPUTER ASSISTED DIAGNOSIS

A. G. Gale, E. J. Roebuck and B. S. Worthington

Academic Department of Radiology, Queen's Medical Centre, Nottingham

At present, some 2500–3000 mammograms a year are performed locally, and upon radiological examination a number of these women are then sent for biopsy. Approximately half these patients have a benign lesion or are normal; the remainder have a malignant pathology. The former patients, therefore, are needlessly diagnosed as requiring a biopsy, with consequent cost to the hospital's resources. This paper describes a new approach to ascertaining the need for a biopsy or follow-up through the use of a microcomputer which permits the radiologist to make a computer assisted diagnostic decision.

We have found that the system results in significantly fewer false positive diagnoses, which should reduce the number of unnecessary biopsies, while producing little variation in correct diagnostic decisions for cancer, compared with normal mammographic reporting. This paper describes the system as well as its current clinical evaluation, and addresses some of the difficulties which arise in codifying image descriptors for use with the program.

AUTOMATIC EVALUATION OF DYNAMIC RADIONUCLIDE STUDIES USING PRINCIPAL COMPONENTS ANALYSIS

K. S. Nijran and D. C. Barber

Department of Medical Physics and Clinical Engineering, Royal Hallamshire Hospital, Sheffield

Quantitative assessment of many dynamic radionuclide investigations generally involves the computation of a time–activity curve (TAC) for the structure (organ) of interest. This is widely performed using the manual region-of-interest (ROI) method. A TAC constructed from a ROI over the organ is corrected for activity attributed to structures underlying and overlapping that organ, *i.e.* for background activity. The background activity is estimated from a second ROI. Problems associated with the manual method are obvious. (1) The background region selected may not be a true representation of the extra-organ activity. (2) The method is operator-dependent, since the ROI has to be selected manually.

A method termed the "intersection method" (IM) which uses principal components analysis, is presented here as an alternative to the manual method The IM overcomes the major problems associated with the manual method The potential of the IM lies in that *a priori* physiological information is incorporated into the data processing, using suitable physiological models. No background correction is involved. The careful isolation of an organ from other surrounding body structures by means of ROI is not required. The method is potentially operator-independent In effect, the analysis can be automated and is significantly faster than the manual method The IM has been applied to dynamic studies of the kidney and the liver with encouraging results

UTILITY OF THE EARLY ACQUISITION OF DATA

I. R. Young, J. A. Payne, S. Khenia and *G. M. Bydder

*Hirst Research Centre, GEC Research Limited, Wembley, Middlesex and *NMR Unit, Hammersmith Hospital, London*

The possibility of there being useful information in the rapidly decaying signals of tissues with short T_2 (or tissues with a fast component) requires that sequences be adapted to acquire data as early as possible. While some of the early back-projection methods allowed data to be taken immediately after slice selection rephasing, this has proved to be difficult with two dimensional Fourier transform methods. The earliest time after which a spin echo can be formed is perhaps 5–10 ms, and it is difficult to do better with a conventional field echo However, it is possible to convert the system to be essentially a single sided one, with echo formation immediately adjacent to the end of phase encoding By increasing gradient sizes the delay from the end of excitation can be reduced to below 5 ms. Signals from tissues such as cartilage are very well seen under such circumstances, and since the method can be used in conjunction with short tau inversion recovery (STIR) encoding, it is possible to cancel fat signals in tissues such as bone marrow, further to enhance contrast

MODALITY INTERFACE AND NETWORKING

R. Bader

Royal Corporation, San Jose, California, USA

The advent of digital modalities has contributed to an information-explosion problem at most hospitals Imaging modalities present a significant cross-section of diagnostically significant images However, the images often cannot be found. Either the images are located away from the prime health-care site where the clinician cannot easily view them, or the history and images concerning a patient are located in the archives external to the hospital, where they are difficult to reach In addition to the difficulty in handling images, proper recording of digital images for off-line reading is difficult.

The ideal solution is to maintain the digital information in its imaged form, rather than compromise dynamic range by capturing the image on film. The need to train large numbers of radiologists through a technique called "over-reading" or through remote fellowships for radiologists in new digital modalities, as well as the ability and techniques of modern electronic equipment to move images and digital data from place to place, are explained.

DATA STORAGE EFFICIENCY AND INFORMATION REDUNDANCY IN DIGITAL IMAGES. AN ANALYSIS AND PRACTICAL APPROACH TO IMPROVEMENT FOR CLINICAL SITES IN COMPUTED TOMOGRAPHY

C. J. Moore

Regional Department of Medical Physics and Bioengineering, Christie Hospital and Holt Radium Institute, Manchester

The increasing number of data generated by digital imaging devices makes it essential to find ways of reducing storage and improving access to archives. Currently, archiving is performed by storing all of the data in an image without discrimination Additionally, data continue to be stored so that they are suited to direct grey-scale display and observation, even though numerical processing can reduce the volume of data and produce data formats that are related to the medical information content of images.

The results of an analysis of computed tomographic image archives aimed at improving data storage are presented It is shown that large portions of reconstruction field data do not depict anatomical detail and are completely redundant. Therefore, they can be discarded prior to compression of the remaining data by a process of redundancy reduction. Unlike simple compression processes, such a reduction exploits the repetition of information typical of grey-scale images Some processing schemes have been suggested that yield apparently impressive storage reductions However, these are generalised techniques that introduce unpredictable errors into the processed image data. Information is deliberately sacrificed to improve data reduction However, this is unacceptable for diagnostic purposes where error-free techniques are required in order to preserve the full information content of the original image.

An error-free process using Huffman, or entropy, coding of the image data is presented as a means of achieving efficient data storage This technique utilises the statistical information found in the images forming an individual clinical investigation An extension of this approach is introduced which classifies an investigation as a member of one of several types of investigation for specific clinical imaging sites. Prior information concerning these sites is then used to specify an efficient form of image data storage.

A SYSTEM FOR THE PRODUCTION OF FLEXIBLE FILM IMAGE FORMATS FROM A COMPUTER DISPLAY

C. P Wells and P. J. Mountford

Department of Medical Physics, Kent & Canterbury Hospital, Canterbury, Kent

An interface has been developed which allows clinical images, graphs and text displayed on a video monitor to be recorded on 8" × 10" X-ray film under computer control Several of these images can be recorded on one film in different formats to form a single report, and these images can be presented in various sizes, even with overlap, without degradation These features do not appear to be available on commercial systems. An outline description of the interface is given together with fuller details of the principles behind those stages which produce the high degree of flexibility of the system. The flexibility is illustrated with some nuclear medicine studies The system has been designed such that with the minimum number of adjustments, the system may be used with nuclear medicine, CT, MRI or any imaging modality which involves the use of a computer and a video display.

A NEW DISPLAY TECHNIQUE FOR COMPUTED TOMOGRAPHIC SCANS BASED ON HISTOGRAM EQUALISATION

P. F. Wankling and J. A. Newell

Department of Medical Physics, Queen Elizabeth Medical Centre, Birmingham

Computed tomographic scans are frequently reported from hard-copy film. A consequence of this is that much of the available information within the image data is not presented to the radiologist since it falls outside the limits of the window setting used. Various windowing and histogram equalisation techniques for grey-scale assignment have been investigated. These were aimed at producing a CT image which presented a wider range of CT numbers at a single window setting, without losing important low contrast detail. This "overview" image may be used, together with the normal image, for diagnosis. Following a comparison of these techniques, which all have attendant disadvantages, a new method has been developed in which histogram equalisation is first applied to the image and the result is then subtracted from the original image. This gives a display of the full range of tissue types, from lung to dense bone, while still retaining the low contrast enhancement of large homogeneous areas that is achieved by histogram equalisation alone. The technique has been implemented on an IGE 8800 CT scanner, and a reasonably fast processing time is achieved. Its effectiveness is being evaluated by radiologists. This technique will also have application in radiotherapy planning using CT data.

THREE-DIMENSIONAL COMPUTED TOMOGRAPHIC REFORMATIONS IN THE ASSESSMENT OF CONGENITAL CRANIOFACIAL ANOMALIES

J. E. Gillespie, I. Isherwood, *G. Barker,
†C. Bannister and †J. Lendrum

*Department of Diagnostic Radiology, Stopford Building, University of Manchester, *University Dental Hospital of Manchester and †Department of Neurosurgery and Plastic Surgery, Booth Hall Children's Hospital, Manchester*

The radiological evaluation of congenital craniofacial anomalies has traditionally been made from the study of standard and cephalometric radiographs. Such radiographs suffer from the disadvantage of superimposition of bony structures. This is a particular problem in the presence of asymmetric deformities. Accurate head positioning may also be difficult when dealing with infants or unco-operative patients. Computer software to facilitate the production of three-dimensional (3D) reformations from a series of conventional CT slices is being used for the evaluation of such bone and soft-tissue abnormalities. These reformations have the advantage of displaying anatomical structures in a conventional and easily assimilated format. Images can then be produced demonstrating the reconstructed volume in multiple orientations without superimposition of structures. Distance between any spatial co-ordinates can be measured.

Twenty examinations have been conducted in a protocol designed to assess the role of 3D CT reformations in the evaluation of congenital craniofacial abnormalities affecting children and adults. The results of this study and our experience of 3D imaging are presented.

Gastrointestinal Radiology

Chairman: Dr J. O. M. C. Craig

Diagnostic techniques for parotid disease, by Mr M. Partridge, Mr J. D. Langdon, Dr S. Rankin and Dr A. Borthwick-Clarke
The evaluation of bowel preparation—three methods compared, by Dr S. Panditaratne and Dr A. H. Chapman
The "bald" duodenum (loss of mucosal folds), by Dr T. Eyre and Dr J. P. Virjee
Sigmoid volvulus—decompression under radiological control, by Dr A. H. Chapman and Dr M. McNamara
The accuracy of double-contrast barium enema in the evaluation of colonic strictures, by Dr C. Hamilton-Wood and Dr J. P. Virjee
Ischaemic colitis—towards earlier detection, by Dr J. P. Virjee
Relationship between gastric emptying and superior mesenteric blood flow following a solid meal, by Dr M. I. Qamar, R. Mountford, P. C. Jackson, Professor E. Rhys Davies and A. E. Read
Linear filling defects on cholangiography, by Dr D. Martin
CT of the gallbladder wall, by Dr R. Whitehouse and Dr D. Martin
DSA in treatment of liver malignancies by temporary intra-arterial microembolisation, by Dr E. Mangel, Dr R.-W. Kenn, Dr R. Huber, Dr B. Eibl-Eibesfeld and Dr K. J. Pfeifer
In vitro echographic studies on colon and rectum, by Mr J. Beynon, Dr D. M. Foy, Dr L. N. Temple, Dr J. P. Virjee and Mr N. J. McC. Mortensen
Rectal bleeding—flexible sigmoidoscopy vs barium enema, by Dr A. Booth and Dr J. P. Virjee
Per-rectal ultrasound in the staging of rectal cancer, by Mr J. Beynon, Dr A. Roe, Dr D. M. A. Foy, Dr L. N. Temple, Mr N. J. McC. Mortensen and Dr J. P. Virjee

DIAGNOSTIC TECHNIQUES FOR PAROTID DISEASE

M. Partridge, J. D. Langdon, S. Rankin and A. Borthwick-Clarke

King's College Hospital, London

A variety of conditions may present with swelling in or around the parotid gland. In most cases the clinical pattern is sufficiently characteristic to allow diagnosis, although special investigations may be necessary to distinguish between inflammatory and neoplastic disease. Sialography is well established as the investigation of choice for chronic inflammatory disease, autoimmune disease and duct obstruction and may be performed as part of the routine assessment of a parotid mass. However, retrospective review has shown that many sialograms are unnecessary, as they seldom influence clinical decisions. When the origin of the lesion is in doubt, sialography is of only limited value in determining whether a lesion is intrinsic or extrinsic to the gland. With CT the distinction between gland and adjacent soft tissue is greatly improved. Deep lobe tumours are as easy to visualise as superficial. Computed tomography cannot predict reliably whether a lesion is benign or malignant, but may show spread beyond the gland capsule or metastatic deposits. The role of ultrasound in parotid disease has yet to be fully established. The technique appears to be quite sensitive in the detection of focal lesions. Results of these investigations are presented.

THE EVALUATION OF BOWEL PREPARATION: THREE METHODS COMPARED

S. Panditaratne and A. H. Chapman

St James's University Hospital, Leeds

Three methods of evaluating Picolax (sodium picosulphate and magnesium oxide, Ferring Pharmaceuticals) as a bowel preparation were compared. One thousand and fifty patients attending for barium enema examinations were divided into three equal groups. One group was questioned as to the effectiveness of the bowel preparation. The second group had a plain abdominal radiograph taken prior to the barium enema which was examined for the presence of faeces (Harned et al, 1980). The third group was given 56 g (2 ounces) of barium to mix with water and drink prior to the bowel preparation and a plain abdominal radiograph was again obtained before the examination in the hope that any residual faeces would be coated with barium (Short, 1980). Failure to determine the status of the patient's bowel preparation occurred in 15% in Group 1 (questioned), 10% in Group 2 (plain radiograph) and 13% in Group 3 (barium, plain radiograph). Picolax alone resulted in inadequate bowel preparation in 14% of patients. Giving barium prior to the bowel preparation failed to improve the accuracy in predicting colon preparation. There was a 5% difference between the plain-radiographic evaluation of the bowel preparation and that obtained by questioning the patient. The avoidance of an unnecessary examination was, therefore, achieved at a cost of 20 plain radiographs.

REFERENCES

HARNED, R. K., WOLF, G. L. & WILLIAMS, S. M., 1980. Preliminary abdominal films for gastrointestinal examinations: how efficacious? *Gastrointestinal Radiology*, *5*, 343.

SHORT, W. F., 1980. Use of a tracer dose of barium for evaluating bowel preparation. *Gastrointestinal Radiology*, *5*, 67.

THE "BALD" DUODENUM (LOSS OF MUCOSAL FOLDS)

T. Eyre and J. P. Virjee

Department of Radiodiagnosis, Bristol Royal Infirmary

The normal mucosal folds of the duodenal loop were absent in 18 unselected patients referred for barium meals. In conjuncion with other radiological features such as irregular coating, gastric metaplasia, strictures, ulcers, lymphoid nodular hyperplasia and the proximal small intestinal appearances, a variety of correct diagnoses was made. These included coeliac disease (with and without histiocytic lymphoma), Crohn's disease, duodenitis, Zollinger-Ellison syndrome and pancreatitis. They were all confirmed endoscopically or clinically. Such mucosal detail can only be obtained routinely if a double-contrast hypotonic technique is used. Interestingly, in many cases where endoscopy was used for confirmation, the macroscopic view was unimpressive. To prevent unnecessary repeat endoscopic examinations for biopsy specimens, it should be routine practice to biopsy all "bald" duodenums irrespective of the endoscopist's opinion at the time of the examination.

SIGMOID VOLVULUS: DECOMPRESSION UNDER RADIOLOGICAL CONTROL

A. H. Chapman and M. McNamara

St James's University Hospital, Leeds

Five patients suspected clinically and on plain-film radiography of having a sigmoid volvulus had the diagnosis confirmed by a water-soluble contrast enema. At the end of this examination a flatus tube was safely passed under radiological guidance and the colon was successfully decompressed in all five patients allowing surgery to be postponed until the patients' general condition had improved. In two patients the colon spontaneously devolved within 24 h, and as they were considered poor operative risks, they were discharged home with no further treatment. In these two patients there is a risk that the volvulus will recur, but it was felt justifiable to accept this risk as they were thought to be unfit for abdominal surgery.

THE ACCURACY OF DOUBLE-CONTRAST BARIUM ENEMA IN THE EVALUATION OF COLONIC STRICTURES

C. Hamilton-Wood and J. P. Virjee

Department of Radiodiagnosis, Bristol Royal Infirmary

To assess the accuracy of double-contrast barium enema (DCBE) in defining the nature of a colonic stricture, 117 patients with such a lesion shown on DCBE were followed up, and their subsequent findings at colonoscopy, laparotomy, histology or autopsy where applicable, were studied. Of these 117 patients, the incorrect or incompletely diagnosed lesions totalled 13, giving an overall accuracy of 88.7%, carcinoma being the predominant cause. In the subpopulation of 49 patients who had been subjected to both DCBE and colonoscopy, no statistically significant difference was found in the accuracy of either investigation in its ability to differentiate a benign from a malignant lesion, DCBE gave an accuracy of 92% and the colonoscopist's visual accuracy at the time of the examination (*i.e.* before availability of histology) was 88%. This latter figure was boosted to 95.8% after histology, from biopsy or brushings, became available.

ISCHAEMIC COLITIS: TOWARDS EARLIER DETECTION

J. P. Virjee

Department of Radiodiagnosis, Bristol Royal Infirmary

Seven cases, clinically unsuspected of having ischaemic colitis, are used to demonstrate the changes in the colon prior to the development of classical diagnostic thumbprinting. All these patients had profuse rectal bleeding over a very short period, investigated by barium enema. None re-bled and subsequent barium studies demonstrated a return to normality or the development of strictures or pseudodiverticula. The cases show that the sequence of events is initial narrowing of the affected segment followed by granular mucosa in this affected oedematous segment. As ischaemia continues, localised oedema results in polypoidal swelling and ulceration, and it is only when coalescence of the polypoidal swellings in the affected segment occurs that we recognise the classical thumbprinting described in ischaemic colitis. To recognise these signs it is important to use a hypotonic agent or narrowing may be misconstrued as being due to temporary spasm. It is also essential to use a double-contrast technique and a well prepared colon as detailed inspection of the mucosa is necessary to evaluate and appreciate the early signs described. With this attention to detail in technique, and evaluation of the mucosal changes, it is possible to diagnose ischaemic colitis prior to thumbprinting and also to differentiate ischaemic changes from other causes of colitis and thumbprinting (ulcerative colitis, Crohn's disease, pneumatosis intestinalis, paracolic diverticular abscess, endometriosis and secondary deposits).

RELATIONSHIP BETWEEN GASTRIC EMPTYING AND SUPERIOR MESENTERIC ARTERY BLOOD FLOW FOLLOWING A SOLID MEAL

M. I Qamar, R. Mountford, P. Jackson, E. Rhys Davies and A. E. Read

Departments of Medicine, Radiology and Medical Physics, Bristol Royal Infirmary, Bristol

Feeding increases the superior mesenteric artery blood flow (SMABF) and induces different types of motor activities in the alimentary canal. The relationship between these two functional aspects in terms of the effect of gastric emptying on intestinal blood flow is still unclear. The present study was designed to investigate whether the post-prandial SMABF was related to the rate of gastric emptying.

Nine healthy male subjects were given a scrambled-egg solid meal labelled with ^{99}Tc^{m}-sulphur colloid. Gastric activity was recorded using a gamma camera over a period of 90 min. Simultaneous serial measurements of SMABF were performed using a recently introduced transcutaneous Doppler ultrasound method (Qamar et al, 1985). There was a significant positive correlation between the gastric emptying rate and post-prandial SMABF in all subjects in the first 60 post-prandial minutes (r varied from 0.8 to 0.98, $p < 0.05$–0.0005). The average slope of all regression lines was within ±2 SE of the slope, indicating that the correlation was similar in all subjects. This correlation was lost when measurements were considered over the 90 post-prandial minutes. These results indicate that a causal connection between gastric emptying and post-prandial intestinal blood flow is very unlikely and that gastric emptying does not play an important role (if any) in modulating post-prandial superior mesenteric artery blood flow.

REFERENCE

Qamar, M. I., Read, A. E., Skidmore, R., Evans, J. M. & Wells, P. N. T., 1985. Gastrointestinal blood flow in man determined by Doppler ultrasound technique. In *WFUMB 85, Proceedings of the Fourth Meeting of the World Federation for Ultrasound in Medicine and Biology and the First World Congress of Sonographers, Sydney, Australia*. Ed. by R. W. Gill & M. J. Dadd (Pergamon Press, London, New York), p. 164.

LINEAR FILLING DEFECTS ON CHOLANGIOGRAPHY

D. Martin

Department of Diagnostic Radiology, University of Manchester

Filling defects seen on cholangiography are most commonly due to gallstones or malignant disease but are rarely of linear form. A retrospective review of 140 cholangiograms demonstrated linear filling defects in 37 patients. These were classified as: (1) admixture defects, where the linear lucency resulted from inadequate mixing of contrast medium and bile-duct contents, (2) mucosal, where focal mucosal abnormality was present, or (3) luminal. Eighteen patients had admixture defects. These occurred in dilated or non-dilated ducts with or without concomitant stones or malignant disease. Admixture defects were usually seen during the early stages of bile-duct filling and were easily recognisable. Further injection of contrast medium and radiographs demonstrated no consistent defect. Mucosal filling defects occurred in 14 patients, most commonly with dilated ducts and common duct stones. Mucosal defects occurred where a previously dilated duct was decompressed and collapsed, leaving redundant, longitudinal mucosal ridges or where a T-tube had previously been present. Luminal linear filling defects were present in five patients. In four the defect was due to gallstones and in one, due to a detached T-tube fragment. Linear defects on cholangiography are common, most frequently resulting from inadequate mixing of bile and contrast medium but often representing mucosal or luminal abnormalities.

COMPUTED TOMOGRAPHY OF THE GALLBLADDER WALL

R. Whitehouse and D. Martin

Department of Diagnostic Radiology, University of Manchester

Contrast enhancement of the normal gallbladder wall on CT has not been adequately studied. Normal gallbladder wall thickness on CT has been variably stated as less than 1 mm, 2 mm or 3 mm. In a retrospective study of 116 patients who underwent pre-contrast and dynamic sequential post-contrast CT examination of the abdomen, a group of 48 patients with no clinical evidence of biliary disease and a further 15 patients with chronic pancreatitis were examined. The attenuation and thickness of the free gallbladder wall was measured before and after contrast. In the clinically normal patients, mean gallbladder wall attenuation pre-contrast was 25 HU and post-contrast 42 HU, with a wall thickness of 1.9±0.43 mm. In patients with chronic pancreatitis these values were 24 HU, 44 HU and 2±0.54 mm, respectively. The enhancement is significant in both groups but there is no statistical difference in the pre- or post-attenuation characteristics, or thickness, of the gallbladder wall between normal patients and those with chronic pancreatitis. We conclude that gallbladder wall enhancement on post-contrast CT is normal and remains normal in patients with chronic pancreatitis. Gallbladder wall thickness is unaltered in patients with chronic pancreatitis, a normal thickness being below 3 mm.

DIGITAL SUBTRACTION ANGIOGRAPHY IN TREATMENT OF LIVER MALIGNANCIES BY TEMPORARY INTRA-ARTERIAL MICROEMBOLISATION

E. Mangel, R. W. Kenn, R. Huber, B. Eibl-Eibesfeld and K. J. Pfeifer

Chirurgische Universitatsklinik Innenstadt, Department of Radiology, Munich, West Germany

Non-resectable malignant lesions in the liver have a poor prognosis. Systemic chemotherapy has little effect on tumour growth. We use repeated, prolonged, DSA-controlled arterial microembolisation with enzymatically degradable starch microspheres alternating with hepatic artery infusion chemotherapy.

After pre-operative angiographic localisation of the liver vessels an arterial access system (Port-A-Cath) is implanted subcutaneously. The prolonged microembolisation is performed via the implanted port, one embolisation cycle lasting 140 min. To determine the number of microspheres needed for complete occlusion, repeated control angiography is necessary. Because of the low flow rate, a Digitron II (Siemens) is used for this purpose. Thirteen patients undergoing this treatment are now being observed for a longer period. During the complete prolonged occlusion, pain and cardiopulmonary changes make intubation narcosis and haemodynamic monitoring obligatory. Apart from the embolisation cycles, the therapy is on an outpatient basis.

IN VITRO ECHOGRAPHIC STUDIES ON COLON AND RECTUM

J. Beynon, *D. M. A. Foy, †L. N. Temple,
‡J. P. Virjee and N. J. McC Mortensen

*Departments of Surgery, *Medical Physics, †Pathology and ‡Radiology, Bristol Royal Infirmary*

An understanding of the ultrasonic image produced by the microanatomy of the large bowel is essential in the expanding field of endoluminal rectal ultrasound. The appearances of normal rectum and colon have been studied *in vitro* to aid the interpretation of invasion in rectal cancer.

Echographic studies have been performed on 15 fresh operative specimens using an ultrasound scanner type 1846 (Bruel and Kjaer, Denmark) with 5.5 MHz and 7.0 MHz transducers. Five distinct layers have been identified Ultrasonic images obtained after sequential removal of the layers of the bowel wall have been compared with the histological findings The first layer (echogenic) corresponds to the mucosa, the second (echopoor) layer to muscularis mucosae, the third (echogenic) layer to submucosa, the fourth (echopoor) layer to muscularis propria, and the fifth (echogenic) layer to the serosa/para-rectal fat. Occasionally a thin, incomplete, echogenic layer has been observed separating the two parts of the muscularis propria layer in the rectum

Definition of the ultrasonographic anatomy of the rectum has enabled accurate assessment of invasion pre-operatively in rectal tumours

RECTAL BLEEDING: FLEXIBLE SIGMOIDOSCOPY VERSUS BARIUM ENEMA

A. Booth and J. P. Virjee

Department of Radiodiagnosis, Bristol Royal Infirmary

The ability to detect pathology by flexible sigmoidoscopy (done by committed colonoscopists) and by double-contrast barium enemas (checked by a consultant) was compared. A total of 83 patients was studied, the major clinical feature being rectal bleeding. The pathologies subdivided into polyps, diverticular disease, carcinomas, and inflammatory bowel disease. Of 26 patients with polyps, both imaging techniques failed to detect five polyps. Radiologically only one of these measured in excess of 1 cm, whereas of those not detected by endoscopy four were over 1 cm in diameter. Surprisingly, the presence of concomitant diverticular disease with these polyps was not endoscopically appreciated in eight patients

Diverticular disease, its association with strictures, and the diagnosis of the aetiology of strictures was made with significantly greater accuracy radiologically. Five mild strictures of the sigmoid were traversed, and hence missed with the colonoscope. Two false positive strictures, presumably due to intense persistent spasm, were also colonoscopically reported. Twelve carcinomas were demonstrated radiologically; four of these not having been seen endoscopically. In eight cases of proctocolitis, one radiologically false negative and one endoscopically false positive proctitis were recorded. In addition, one case of Crohn's disease was thought, endoscopically before biopsy assessment, to be a carpeting villous tumour.

The importance of a double-contrast barium enema, especially in rectal bleeding, is confirmed. Reasons for the limitations exposed in this study are discussed and the value of flexible sigmoidoscopy as opposed to rigid proctosigmoidoscopy, is questioned.

PER-RECTAL ULTRASOUND IN THE STAGING OF RECTAL CANCER

J. Beynon, A. Roe, *D. M. A. Foy, †L. N. Temple,
N. J. McC. Mortensen and ‡J. P. Virjee

*Departments of Surgery, *Medical Physics, †Pathology and ‡Radiology, Bristol Royal Infirmary*

Local invasion and para-rectal lymph-node involvement in rectal cancer is currently assessed by digital examination, which is highly subjective and related to surgical experience. Using an ultrasound scanner type 1846 (Bruel and Kjaer, Denmark) the effectiveness of endoluminal sonography in predicting invasion and lymph-node involvement is being evaluated. Rotating 5.5 MHz and 7.0 MHz transducers provide 360° scans of the rectum and para-rectal tissues.

Examinations have been performed on 42 primary rectal cancers and results compared in 37 cases with histopathological findings and in three cases with laparotomy observations. Local invasion was graded according to the UICC classification. Sonographically five cases were T1, eight cases T2, 25 cases T3 and four cases T4 The coefficient of correlation between sonographic and histopathological findings was 0.92 ($P < 0\ 001$) Invasion beyond the muscularis propria was predicted with a sensitivity of 96% and specificity of 92%, and had a predictive value of 96%. Lymph-node involvement was predicted in 17 cases. Correlation with histopathology revealed the technique to have a sensitivity of 92%, specificity of 73%, and predictive value of 65%.

Endoluminal ultrasound staging of rectal cancer is more accurate than digital evaluation and its use pre-operatively aids the planning of subsequent treatment

Proceedings of The British Institute of Radiology

Pelvic Afterloading

Chairman: Professor C. A. Joslin

High dose-rate brachytherapy using ^{60}Co sources in the treatment of cancer of the uterine cervix, by Dr A. J. Subandono, Tj Kuipers, S. K. The and J. H. Meerwaldt
The radiobiology of changes in dose-rate, by Dr R. G. Dale
Pathology of the late effects in the bowel following pelvic afterloading, by Dr N. Carr, P. F. Schofield and B. R. Pullan
Isodose calculations during afterloading, by Mrs S. E Batey
Has afterloading improved radiation protection? by Dr C. H. Jones, A. M. Bidmead and W. Anderson
Should we encourage afterloading in developing countries? by Dr B. M. Hancock
How can we adapt afterloading to other sites? by Mr E. Van't Hooft

HIGH DOSE-RATE BRACHYTHERAPY USING COBALT-60 SOURCES IN THE TREATMENT OF CANCER OF THE UTERINE CERVIX

A. J. Subandono, Tj. Kuipers, S. K. The and J. H. Meerwaldt

The Dr Daniel den Hoed Cancer Centre and Rotterdam Radio-Therapeutic Institute, Rotterdam, The Netherlands

With the presently applied method, external irradiation (23 fractions of 2 Gy without central shielding) is followed by two intracavitary applications of high dose-rate brachytherapy (HDB), each delivering 8.5 Gy at point A. A thin metal chain inserted into the bladder is a better marker for dosimetry than the balloon of a Foley catheter. The rectal anterior wall is visualised by means of a plug with metal markers. The small bowel and the sigmoid colon are filled with contrast medium. The results are compared with those achieved earlier with external irradiation combined with three applications of low dose-rate brachytherapy (LDB) according to the Stockholm method.

The corrected disease-free 5-year survival rates are given for HDB and LDB respectively: Stage I 82%, 80%; Stage II 74%, 66%; Stage III 34%, 44%; Stage IV 20%, 20%, without statistically significant differences between the methods. Local and regional recurrence rates are also similar. Overall grade-3 bowel complications were 6% with both methods, but 3.7% when standard HDB method was applied using a Selectron HDR machine instead of a Cathetron. Overall grade 3 urological complications were 8% with LDB and 4% with HDB, but 0% in the last 31 standard method HDB Cathetron treatments as well as in the first 27 Selectron HDR patients. We conclude that HDB and LDB provide similar curative results. The lowest complication rates were achieved with the standard HDB technique using the Selectron HDR machine. The advantages of the short HDB application times are: a more reliable dosimetry; no long-lasting bed ridden isolation, and possibility of outpatient treatment. This means a decrease of the patient's psychological burden and reduction of the cost of treatment.

THE RADIOBIOLOGY OF CHANGES IN DOSE-RATE

R. G. Dale

Charing Cross Hospital, London

The introduction of afterloading machines which can deliver treatments at very high dose-rates has necessitated a reappraisal of conventional ideas relating to intracavitary dosage. The well known radiobiological models provide useful guidelines (Liversage, 1980) but, even if total doses are adjusted in order to avoid excessive normal tissue reactions, it is still possible for the therapeutic ratio to be less advantageous in the high dose-rate case. A more recent method for assessing radiation effects is by means of the linear-quadratic (LQ) formulation (Fowler, 1984). Development of the basic model (Dale, 1985; Thames, 1985) has enabled the LQ method to be applied also to the analysis of protracted regimes. The extended model can incorporate the effects of differing sublethal recovery rates between tissues, where these are known (Thames et al, 1984).

All LQ formulations include a parameter (the α/β ratio) which is related to the specific type of radiation effect under consideration. In principle, therefore, it is possible to assess any treatment in terms of the differential radiation response between tissues. The LQ model may thus be capable of providing new insights when comparing the effectiveness of high and low dose-rate schedules.

REFERENCES

DALE, R. G., 1985. The application of the linear-quadratic dose-effect equation to fractionated and protracted radiotherapy. *British Journal of Radiology, 58,* 515–528.

FOWLER, J. F., 1984. Review: Total doses in fractionated radiotherapy. *International Journal of Radiation Biology, 46,* 103–120.

LIVERSAGE, W. E., 1980. A comparison of the predictions of the CRE, TDF and Liversage formulae with clinical experience. *British Journal of Radiology, Special Report 17,* 182–189.

THAMES, H. D., WITHERS, H. R. & PETERS, L. J., 1984. Tissue repair capacity and repair kinetics deduced from multifractionated or continuous irradiation regimes with incomplete repair. *British Journal of Cancer, 49, Supplement VI,* 263–269.

THAMES, H. D., 1985. An "incomplete repair" model for survival after fractionated and continuous irradiations. *International Journal of Radiation Biology, 47,* 319–339.

PATHOLOGY OF THE LATE EFFECTS IN THE BOWEL FOLLOWING PELVIC AFTERLOADING

N. D. Carr, *P. F. Schofield and †B. R. Pullan

Department of Surgery, Whittington Hospital, London,
**Department of Surgery, Withington Hospital, Manchester and*
†Department of Medical Biophysics, University of Manchester

Occlusive changes in the small intramural blood vessels are commonly found at the sight of radiation bowel disease (RBD) (Berthrong & Fajardo, 1981). It has been suggested that these vascular lesions may obliterate the microvasculature of the bowel and lead to progressive ischaemia (De Cosse et al, 1969). Although there is evidence from microvascular studies in experimental animals to support this hypothesis (Eriksson 1982), the role of small vessel disease in human RBD remains unclear.

The microvasculature has been investigated in the normal bowel of 45 patients and in the bowel of 18 patients with late complications after pelvic radiotherapy administered for carcinoma of the uterine cervix or bladder. Tissue samples from post-operative colectomy specimens in which the intramural vasculature had been perfused with barium sulphate suspension (Micropaque, Nicholas Laboratories) immediately after surgical removal were examined. Microradiography was used to study intramural vascular pattern which was abnormal in RBD. Structures were associated with a transmural reduction in vascularity, while areas of bowel adjacent to perforations, necrosis and fistulae exhibited zones of complete avascularity, affecting all or part of the wall. An X-ray fluorescence system was used to estimate barium concentration and hence microvascular volume (Carr et al, 1984). The irradiated group showed a highly significant reduction in barium concentration ($P < 0.001$) when compared with the control group. If either intracavitary or external radiotherapy alone was administered, a relatively short segment of bowel displayed reduced microvascular volume. More usually, combined intracavitary and external radiotherapy were used and the length of bowel involved was much greater.

It is concluded that microvascular compromise is an important factor in the pathogenesis of human RBD.

REFERENCES

BERTHRONG & FAJARDO, C., 1981. Radiation injury in surgical pathology. *American Journal of Surgical Pathology, 5,* 153–178.

CARR, N. D., SCHOFIELD, P. F. & PULLAN, B. R., 1984. A method for the determination of microvascular volume in tissue samples. *Clinical Physics and Physiological Measurements, 5,* 21–27.

DE COSSE, J. J., RHODES, R. S. & WENTS, W. B., 1969. The natural history and management of radiation induced injury of the gastrointestinal tract. *Surgery Annual, 170,* 369–384.

ERIKSSON, B., 1982. Microangiographic pattern in the small intestine of a cat after irradiation. *Scandinavian Journal of Gastroenterology, 7,* 887–895.

ISODOSE CALCULATIONS DURING AFTERLOADING

S. E. Batey

Department of Medical Physics, Royal Sussex County Hospital, Brighton

The advent of low dose-rate afterloading equipment and computerised treatment planning systems has made the production of individual treatments for each patient theoretically possible. By supplementing conventional radiographs with CT scan information, a suitable intracavitary treatment can be decided on the basis of the dose distribution in important anatomical structures. Combined intracavitary and external beam treatments can be similarly evaluated.

In practice, such complete individualisation would be difficult to achieve due to constraints on time and resources, and standard source loading patterns and treatment times can be satisfactorily utilised for most patients. Point doses or a complete distribution may be calculated at any of the following times:

(1) before loading the applicators;
(2) during an insertion;
(3) between insertions;
(4) after the intracavitary treatment has been completed for reference purposes or for summating with external beam irradiation.

The most appropriate procedure has to be decided for each patient and type of treatment regime.

In Brighton, a routine regime for the treatment of cancer of the cervix is three Selectron insertions followed by external beam irradiation. For this regime the following procedure has been adopted. After each insertion, point bladder and rectal doses are calculated using orthogonal radiographs and subsequent insertions may be modified after consideration of these doses. After the intracavitary treatment has been completed, the total distribution is superimposed on appropriate CT slices and the proposed external beam arrangement adjusted to obtain the best combined plan.

HAS AFTERLOADING IMPROVED RADIATION PROTECTION?

C. H. Jones, A. M. Bidmead and W. Anderson

Joint Department of Physics, Institute of Cancer Research and the Royal Marsden Hospital, London

In recent years ^{137}Cs and other radionuclides have replaced radium as radiation sources for plesiotherapy and endotherapy techniques. As a consequence it has become possible to develop more effective afterloading techniques to reduce exposure of personnel to ionising radiation. Afterloading techniques have been developed for intracavitary methods of treatment and also for implanting rigid or flexible interstitial radiation sources. In this paper we consider the use of manual and low dose-rate automatic afterloading techniques that are being used for treating gynaecological disease, with an emphasis on the use of the low dose-rate Selectron. Attention is paid to the changes in personnel exposure doses due to the introduction of afterloading as well as the advantages and problems of these procedures and the cost of their implementation.

SHOULD WE ENCOURAGE AFTERLOADING IN DEVELOPING COUNTRIES?

B. M. Hancock

Christie Hospital, Manchester

In developing countries cancer causes only 3.7% of deaths, but of these cancers, carcinoma of the cervix is the commonest. Third-world doctors want to use the latest technology. The medical and nursing staff want to reduce their own radiation doses, just as we do in the West. Therefore remote afterloading might seem a reasonable buy for the Third World.

The ICRP requires that radiation exposure should be "as low as reasonably achievable" but the Commission adds "economic and social factors being taken into account." In the Third World, economic and social factors are obviously vastly different from those in the West. Not only are many countries extremely poor, but their pattern of disease is different from ours. Many people, especially children, die from conditions which could be prevented or cured with minimal expenditure.

The benefits of afterloading are examined in relation to radiation protection. The radiation risk is small $1.25 \times 10^{-2}\ \mathrm{Sv}^{-1}$ for induction of fatal cancers, and $0.80 \times 10^{-2}\ \mathrm{Sv}^{-1}$ for induction of hereditary effects. At the Christie Hospital, when 400 cervix patients a year were treated with manually loaded radium and nursed in the open ward, the annual collective dose to staff was 1.13 man-Sv. The cost of the Selectron afterloading system is £94 000 for one machine and 36 sources. There are housing, staffing and maintenance costs as well.

If a developing country is interested in better health for all its people, rather than protecting staff from a small risk it would be better to spend the money on other projects.

HOW CAN WE ADAPT AFTERLOADING TO OTHER SITES?

E. Van't Hooft

Nucletron, Leersum, The Netherlands

Afterloading is known from the early part of this century, when pre-inserted celluloid tubes of the size of a clinical thermometer were used. It was then easy to introduce successfully a glass radium capsule to be inserted into each tube and retain it there as long as desired. Today we see that more sophisticated equipment is used remotely to transfer radioactive sources from a container into a pre-inserted tube or group of tubes. This does not only eliminate all the unwanted dangerous exposure to hospital staff, but it also gives good control during the treatment, and automatic source return when time elapses. With this new equipment called Selectron, not only is cervical cancer treated, using a low, medium or high dose-rate technique, but also breast implants, rectal impants, head and neck implants, oesophagus, prostate, bile-duct, lung, bladder, etc have become technically feasible. Because of the accurate and local high doses which can now be given to all those sites, new challenges to improve survival, lower complication risks and provide well tolerated, low-cost palliation, have come within reach

Radiotherapy Physics

Chairman: Mr T. J. Godden

A comparison of dosemeters used for *in vivo* measurements during total-body irradiation, by Mr R J. Aukett

Clinical experience with the Royal Marsden Hospital CT simulator applied to planning radiotherapy treatment for breast cancer, by S. Webb, M. O. Leach, R E. Bentley, K. Maureemootoo, M. A. Toms and J. Yarnold

A comparison of measured and calculated dose distributions using the Philips Oncology Support System, by Mr A K Morgan, Dr S C Klevenhagen and Mrs R. A. Lake

Oblique reconstruction of CT scans, by Mr S. C. Bolton and Mr R. J. Aukett

The placing of tissue compensators—on the shell or in the beam? by Mr M. Samarasekara and Dr F. R. Hudson

An integrated shell system, by Mr R. J. Aukett, Mr S. C Bolton and Mr D. Yeomanson

Current techniques in use at Mount Vernon Hospital for the preparation of surface applicators for radiation therapy, by Mr D. Hynd, Mr H. Lockwood and Dr F R. Hudson

The commissioning of the Clinacomp compensator cutter for use with megavoltage photon beams up to 24 MV, by Miss C. S. Abbott and Mr T. J Godden

The design of a maze entrance for a 24 MeV medical linear accelerator facility, by Dr A. Sherwin, Dr D. Gifford and Mr T. J. Godden

A pantograph cutter for the preparation of photon shields, by Mr G R. Plant

A COMPARISON OF DOSEMETERS USED FOR *IN VIVO* MEASUREMENTS DURING TOTAL-BODY IRRADIATION

R. J. Aukett

District Department of Medical Physics & Clinical Engineering, Leicester Royal Infirmary

In total-body irradiation it is necessary to control the dose by direct measurements at a number of points on the surface of the patient. This contrasts greatly with the techniques used in other forms of radiotherapy Normally, semiconductor or thermoluminescent dosemeters are used and considerable variation is often found between readings. The variation in sensitivity of these dosemeters has been measured for different irradiation conditions including depth, orientation, beam size The different dosemeters are compared and techniques for their use are discussed.

CLINICAL EXPERIENCE WITH THE ROYAL MARSDEN HOSPITAL COMPUTED TOMOGRAPHY SIMULATOR APPLIED TO PLANNING RADIOTHERAPY TREATMENT FOR BREAST CANCER

S. Webb, M. O. Leach, R. E. Bentley,
K. Maureemootoo, *M. A. Toms and *J. Yarnold

*Section of Physics and *Section of Radiotherapy, Institute of Cancer Research and Royal Mardsen Hospital*

A radiotherapy simulator has been modified to generate CT reconstructions suitable for radiotherapy treatment planning (Webb et al, 1985) The scanner has been designed to provide a reconstructed field of view of 48 cm diameter and a minimum aperture of 75 cm The scanner makes use of a unique position-sensitive detector based on the use of a plastic scintillator (Webb et al, 1984, Leach et al, 1985) Data collection, processing and reconstruction are accomplished entirely digitally. The role of the "CT simulator" in assisting the planning of post-operative radiotherapy as part of the conservative management of breast cancer is currently being assessed The breast is sectioned, in the treatment position, at three levels corresponding to the mid-plane and upper and lower borders of tangentially applied treatment fields. The study highlights the importance of the differences in patient contour and internal lung borders at these levels. The implications for dosimetry are discussed together with an assessment of the importance of lung inhomogeneity corrections. An earlier clinical study (Webb et al, 1985) demonstrated adequate image quality from this scanner; the importance of the current study lies in our conclusive evidence that planning without multiple level CT obtained in the treatment position can have implications for local control, pulmonary damage and cosmesis

REFERENCES

LEACH, M O., WEBB, S. & BENTLEY, R E., 1985. *Physics in Medicine and Biology, 30*, 303–311

WEBB, S., LEACH, M O., BENTLEY, R. E & YARNOLD, J, 1985 *Medical and Biological Engineering and Computing, 23, (Suppl 2)*, 955–956.

WEBB, S., LEACH, M O & HERMAN, G T., 1984 *IEEE Transactions, Medical Imaging (MI3)*, 193–196

A COMPARISON OF MEASURED AND CALCULATED DOSE DISTRIBUTIONS USING THE PHILIPS ONCOLOGY SUPPORT SYSTEM

A. K. Morgan, S. C Klevenhagen and R. A. Lake

Department of Medical Physics, The London Hospital

The Philips Oncology Support System (OSS) uses a three-dimensional projective beam model, originally developed by Van de Geijn, to calculate photon dose distributions in tissue. These distributions can be for planes in any orientation, making the system ideal for examining dose distributions in planes other than the central plane The beam model makes storage of complete off-axis dose distributions unnecessary, as only central axis percentage depth doses and two perpendicular profiles at one depth for open square fields are required. For wedged fields, only the physical dimensions of the wedges are required, the OSS calculates the attenuation through the wedges and modifies the open-field data This paper presents the results of a comparison of calculated dose distributions with distributions measured in a water phantom. In particular, the effect of surface obliquity and wedges on the three-dimensional distribution has been studied The OSS uses an equivalent-path-length method, in conjunction with the projective beam model, to correct for inhomogeneities. In view of the widespread use of CT data for treatment planning, the accuracy of this method has been assessed by further measurements

OBLIQUE RECONSTRUCTION OF COMPUTED TOMOGRAPHIC SCANS

S. C. Bolton and R. J. Aukett

District Department of Medical Physics & Clinical Engineering, Leicester Royal Infirmary

In radiotherapy planning, it is frequently necessary to use CT views which are oblique to the planes in which the scan was originally made. This may occur either because the machine is unable to scan at the angle required, or because the angle has been changed during the course of planning A program has been written which reconstructs the CT view in a plane at an arbitrary angle to a series of CT slices Three alternative algorithms have been used for the interpolation required in between the slices The results obtained are shown and are compared with views obtained directly

THE PLACING OF TISSUE COMPENSATORS: ON THE SHELL OR IN THE BEAM?

M. Samarasekara and F. R. Hudson

Physics Department, Mount Vernon Hospital, Northwood, Middlesex

The factors affecting the placing of tissue compensators on the shell or in the beam are analysed for low energy beams such as 250 kV and for megavoltage beams. The principal factors to be considered are the importance of skin sparing effects, the choice of compensator material, the accuracy of compensation achieved, and the ease and cost of preparation. Examples of both approaches to compensator preparation are presented showing the advantages and disadvantages of each technique Data are presented to enable the thickness of lead needed for compensator construction to be decided for megavoltage beams The problem of correction for tissue inhomogeneity is discussed and examples of verification experiments are analysed.

AN INTEGRATED SHELL SYSTEM

R. J. Aukett, S. C. Bolton and D. Yeomanson

District Department of Medical Physics & Clinical Engineering, Leicester Royal Infirmary

In radiotherapy of the head and neck it is desirable to obtain as much similarity as possible between the planning CT scan, simulation and treatment of a patient A system is described in which the same shell has successfully been used at all these stages. A means of holding the shell has been designed which can be used with minimal modification on all machines, including CT scanners, and during the marking out stage of planning.

CURRENT TECHNIQUES IN USE AT MOUNT VERNON HOSPITAL FOR THE PREPARATION OF SURFACE APPLICATORS FOR RADIATION THERAPY

D. Hynd, *H. Lockwood and F. R. Hudson

*Physics Department and *Department of Oral Surgery, Mount Vernon Hospital, Northwood, Middlesex*

A regular flow of patients at Mount Vernon Hospital, 23 in 1984, has been assigned to treatment with surface applicators. These patients may be grouped into those with external skin lesions (17) and those with intraoral lesions (6). Techniques for the preparation of applicators are described and illustrated by examples prepared for a range of typical treatment sites. External applicators are now prepared, using thermoplastic material which provides an efficient and effective method for positive localisation. The technique permits the effective afterloading of the activity to minimise the exposure to the staff Intraoral applicators have been prepared by the Department of Oral Surgery, using acrylic applicators made up to the form of dentures. These in particular often provide a means for the treatment of small, but difficult, sites with the minimum tissue volume raised to high dose levels.

THE COMMISSIONING OF THE CLINACOMP COMPENSATOR CUTTER FOR USE WITH MEGAVOLTAGE PHOTON BEAMS UP TO 24 MV

C. S. Abbott and T. J. Godden

Department of Medical Physics, Bristol Radiotherapy and Oncology Centre

The use of compensators in radiotherapy is well recognised. The Clinacomp compensator Cutter has been manufactured to facilitate the construction of compensators using a low melting point lead alloy poured into a Styrofoam mould. This mould is shaped to the patient's contour by moving a stylus over the treatment area A series of mechanical linkages simultaneously reduces and transfers the contour information to a small drill which cuts the Styrofoam to shape. The reduction ratio is determined for each photon energy, field size and depth of dose calculation plane. The results of a study of the effects of compensators on the radiation distribution at different depths in tissue are presented together with details of their possible use over the photon energy range from ^{60}Co photons to 24 MV photons

THE DESIGN OF A MAZE ENTRANCE FOR A 24 MEV MEDICAL LINEAR ACCELERATOR FACILITY

D. Gifford, T. J. Godden and *A. Sherwin

*Bristol and Weston Health Authority and *National Radiological Protection Board, Chilton, Didcot, Oxfordshire*

The installation of a 24 MeV linear accelerator in a treatment room previously housing a 35 MeV betatron required modifications to be carried out to cater for new beam geometry, increased photon yield and adventitious neutron production. Although the neutron yield of a 35 MeV betatron operated in the electron mode does not require specific provision for neutron attenuation, both the different design of the electron accelerating system and the different operating mode intended for the installation under consideration were likely to give rise to neutron levels which would require the provision of appropriate protective measures. Whereas the photon barriers required to produce the necessary degree of attenuation are likely to be sufficient for the purposes of protection against neutrons, in the case of similar installations elsewhere the escape of neutrons down the maze into the control area has been reduced to the appropriate levels by the provision of a door weighing several tons. The provision of such a barrier presents considerable problems both of a practical and of a psychological nature, and in the present case it was decided to attempt to reduce the neutron flux at the maze entrance by the application to the surfaces of the maze of a special shielding material (Premadex) initially developed by the NRPB, the design considerations being established by means of Monte Carlo calculation. Preliminary measurements have indicated the satisfactory nature of this approach.

A PANTOGRAPH CUTTER FOR THE PREPARATION OF PHOTON SHIELDS

G. R. Plant

Department of Medical Physics, General Hospital, Nottingham

A new hot wire cutter and casting technique for the preparation of low melting point alloy beam shaped moulds has been developed. The equipment improves the standard of accuracy and range of application of machine-mounted customised photon shielding for radiotherapy. A pantograph mechanism is used in the section of cutter between the expanded polystyrene mould and the tracing film, translating the vertical geometry of this section to horizontal. This arrangement has produced more accurate moulds due to higher cutting wire tension and ease of tracing movement. Also, the unwieldiness of more conventional types of cutter has been overcome. The unit is mounted on a free-standing bench at normal working height. A new casting technique lessens the occurence of shrinkage voids in the shields. The shields may be customised for treatments at any gantry angle and the finished trays are interchangeable between the three linear accelerators in the department.

Lung Radiology Update

Chairman: Dr P. R. Goddard

The imaging of haemoptysis, by Dr B. Strickland

CT as a quantitative method for assessing radiation injury to the mouse lung, by Dr D. Nicholas and Dr J. D. Down

Diagnostic imaging of post-irradiation changes in the chest, by Dr J. Bell, J. A. Bullimore, Professor E. Rhys Davies, J. Hill and Dr P. R. Goddard

Dengue haemorrhagic fever in the differential diagnosis of pelural effusion, by Dr G. Harverson

Pleural effusion causing unmatched ventilation defects in ventilation/perfusion scanning, by Dr P. R. Goddard, Dr J. Henson and Professor E. Rhys Davies

THE IMAGING OF HAEMOPTYSIS

B. Strickland

Brompton Hospital, London

In the investigation of haemoptysis, a careful history and examination are essential. Bleeding from the upper airways (nose, gums etc.) must be excluded. The most important initial investigation is radiography of the chest. A PA film alone is inadequate. Two high kV films or three standard radiographs are required. Where the chest radiograph is normal, fibre-optic bronchoscopy is indicated in smokers over 40 years old and selective bronchography should be considered via the bronchoscope at the time. Small pulmonary infarcts cause the greatest difficulty in diagnosis, but a positive ventilation perfusion scan is usually diagnostic. Tomography is often neglected where CT is available. It is still a quick, cheap form of special investigation with considerable value.

Computed tomography is invaluable if used in a deductive manner. Each scan must be tailored to the individual problem. Narrow section scans with a special algorithm, possibly with the patient prone or in lateral decubitus, may be required. Full inspiration radiographs and a wide window setting are essential. Pulmonary angiography is rarely of value in pulmonary infarction. its use lies in demonstrating vascular malformations. Bilateral bronchography is still occasionally required, but bronchial arteriography is indicated only where therapeutic embolisation is to be undertaken. Digital subtraction angiography is disappointing in cases of pulmonary disease and NMR has little to offer at the moment.

COMPUTED TOMOGRAPHY AS A QUANTITATIVE METHOD FOR ASSESSING RADIATION INJURY TO THE MOUSE LUNG

D. Nicholas and J. D. Down

Royal Marsden Hospital and Radiotherapy Research Unit, Institute of Cancer Research, Surrey

Computed tomography was performed on the lungs of CBA and C57Bl mice at varying time intervals after 13 Gy and

16 Gy irradiation to the whole thorax. With careful consideration of artefacts associated with lung cross-sectional area and breathing rate, the mean density of the lung was evaluated in Hounsfield units (CT number). In CBA mice, this parameter showed a biphasic increase in lung density with time from irradiation, corresponding to an early phase of radiation pneumonitis and a late phase dominated by pleural effusions. Reduced lung volumes were also seen during the late response and lung compression due to accumulations of pleural fluid is considered a major factor in these observations. C57Bl mice did not develop radiation pneumonitis but appeared to be equally responsive to later radiation-induced increases in lung density. The results obtained from CT-derived densitometry compared well with measurements gained from functional and survival endpoints. Computed tomography provides a sensitive and informative technique for assessing the extent of radiation injury to the mouse lung and is potentially useful for quantifying the counterpart in patients.

DIAGNOSTIC IMAGING OF POST-IRRADIATION CHANGES IN THE CHEST

J. Bell, J. A. Bullimore, E. Rhys Davies, J. Hill and P. R. Goddard

Department of Radiodiagnosis, Bristol Royal Infirmary

The chest radiographs and CT scans of 20 patients who had undergone thoracic irradiation were reviewed. A further 19 patients undergoing irradiation of the thorax were studied prospectively with ventilation-perfusion lung scanning with single-photon emission computed tomography (SPECT), in addition to plain radiography and CT.

Computed tomography was shown to be more sensitive than plain radiography in detecting post-irradiation changes in the lung. In some cases it is also more specific, showing areas of pulmonary opacification to have a straight edge corresponding to the edge of the irradiation field, such an edge is invisible on plain radiography owing to its obliquity. Shrinkage of pulmonary vessels in areas outside the irradiation field is also seen.

Ventilation-perfusion scanning shows that defects occur in lung perfusion which may be partially matched by ventilation defects. Defects occur both within the original irradiation field and outside it. Imaging of the perfusion scans by SPECT shows the defects with a much greater sensitivity than planner scans. Those defects in the irradiation field are matched by CT opacification; those outside the field may be matched by areas of vessel shrinkage. Perfusion defects outside the irradiation field appear to be related to irradiation of the hilum.

DENGUE HAEMORRHAGIC FEVER IN THE DIFFERENTIAL DIAGNOSIS OF PLEURAL EFFUSION

G Harverson

Department of Radiodiagnosis, Bristol Royal Infirmary

Dengue haemorrhagic fever is a mosquito-borne, viral infection of childhood characterised by pyrexia, followed after a few days by severe shock and haemorrhagic manifestations. The child presents with cold extremities and listlessness after 3–6 days' pyrexial illness. Epistaxis, vomiting of altered blood, or presence of blood in stools or urine may be reported. Petechial skin haemorrhages, hepatomegaly, tachycardia and low pulse pressure are found on examination. Marked thrombocytopenia is invariably present, and a 20% rise in haematocrit level is usual. Bilateral pleural effusions were observed in eight children with haemorrhagic fever in central Thailand. These were related to increased capillary permeability, intravenous fluid therapy, and intrapleural haemorrhage. No cardiac or pulmonary abnormality was present. Spontaneous clearing followed clinical recovery.

Dengue haemorrhagic fever is an important cause of bilateral pleural effusions with an otherwise normal chest radiograph in South East Asia. This diagnosis should be considered in febrile children recently resident in the Far East.

PLEURAL EFFUSION CAUSING UNMATCHED VENTILATION DEFECTS IN VENTILATION/PERFUSION SCANNING

P. R. Goddard, J. Henson, E. Rhys Davies

Department of Radiodiagnosis, Bristol Royal Infirmary

In a review of 100 consecutive patients who had ventilation/perfusion scans, 20 had pleural effusion or thickening visible on their plain chest radiographs. Defects of ventilation not matched by perfusion occurred in 13 of the 20. This sign was not observed when the basal opacification was due to pleural thickening and it is believed to be due to the mobility of pleural fluid and the procedure used for imaging.

Injection of Tc-labelled microspheres was given with the patient supine. In this position a mobile effusion lies posteriorly and perfusion allows binding of microspheres in the bases as well as in the remainder of the lungs except posteriorly. Imaging using the gamma camera is carried out in the erect position when the dependent effusion prevents adequate ventilation. This results in a ventilation/perfusion mismatch since the microspheres producing the perfusion image had of course already been fixed. It is important to understand the effects of a pleural effusion on ventilation/perfusion scanning in order that a correct interpretation can be made. The presence of an effusion on the plain chest radiograph will provide an explanation for an unmatched ventilation defect at the same base and other diagnoses such as infection and infarction do not need to be invoked.

Proceedings of The British Institute of Radiology

Digital Radiology Physics

Chairman: Mr J. A. Garrett

Digital greyscale fluorography, by Dr R. C. Fowler, Dr G. Bonsor and Dr D. J. Lintott
Dual energy radiography, by Miss M. Arnold and Mr N. E. Tomlinson
Evaluation of the processing functions of DSA image processors, by Mr K. P. Maher, Dr J. F. Malone, Dr G. D Hurley and Dr D P. McInerney
DSA—a new method for the physical assessment of imaging performance, by Dr N. E. Tomlinson, C. A. Greatorex and C. K. Battye

DIGITAL GREYSCALE FLUOROGRAPHY

R. C. Fowler, G. Bonsor and D. J. Lintott

Department of Radiology, General Infirmary at Leeds

Further evaluation of digital greyscale fluorography (DGF) at the General Infirmary at Leeds is described. Digital greyscale fluorography is an image-intensifier based technique for general digital radiography. It has been developed on a Philips DVI-V unit, and initial results were presented at Radiology '85. Evidence to demonstrate the wide clinical versatility of the system is now presented with examples of a variety of radiological examinations including contrast studies The facility of easy and immediate image manipulation results in a system of effectively wide latitude combined with good contrast sensitivity. The additional application of image processing such as contour enhancement and histogram equalisation extends the scope of the technique and these features are illustrated. The results of a comparative assessment of DGF images and conventional radiographs are presented. In this study, using a chest phantom, the relative conspicuity of simulated pulmonary nodules is assessed and the implications discussed.

An additional application of the technique is digital greyscale angiography, which produces non-subtracted digital angiographic images with the same potential for manipulation and enhancement. This development may remove the need for a conventional camera or film changer as a "back-up" on a digital subtraction angiography unit

DUAL ENERGY RADIOGRAPHY

M. Arnold and N. E. Tomlinson

Guy's Hospital, London

Dual energy techniques in digital subtraction fluorography are generating much interest, because they enable the "soft-tissue" and "bone" components of an image to be represented separately Soft tissue as imaged by a lower kV exposure can be digitally removed from a higher kV image as part of hybrid subtraction. Such sophisticated techniques require an expensive, rapid kV switching generator and powerful computer facilities.

In general radiography, techniques may be aimed at imaging soft tissue using low energy photons, as in mammography, or at imaging calcified high-contrast structures using higher energies The advantage of exposing a radiograph using two energies is that it should be possible simultaneously to include enhanced soft-tissue information not normally represented in the image The principle is being experimentally applied to magnified radiographs of peripheral joints using X-ray tubes with effective focal spot sizes of 0.1 mm down to 5 μm. The resulting images display high detail resolution in patients suffering from various rheumatological conditions As rheumatoid diseases involve the soft tissues, especially cartilage, the soft-tissue visualisation of these radiographs, once enhanced, may contribute additional information with respect to the progress of the disease. This enhancement is achieved in two ways: firstly, the extra low-energy component in the X-ray spectra used means the beam is more heavily attenuated by soft-tissue structures and greater object contrast is generated; secondly, this object contrast is well represented by using a film/screen combination which is sensitive to low energies and produces high image contrast in the final radiograph.

The clinical and diagnostic benefit of this extra image information has yet to be explored. Once dual-energy radiography has been optimised technically, it will then be possible to begin clinical trials. At present the most favourable areas for its use would appear to be rheumatology, the imaging of certain types of tumour, and possibly general chest examinations

EVALUATION OF THE PROCESSING FUNCTIONS OF DIGITAL SUBTRACTION ANGIOGRAPHY IMAGE PROCESSORS

K. P. Maher, J. F. Malone, G. D. Hurley and D. P. McInerney

Department of Medical Physics & Bioengineering and Department of Radiology, Meath/Adelaide Hospitals, Dublin, Ireland

A large number of DSA systems are now commercially available Evaluations of such systems have concentrated on parameters which include spatial resolution, contrast sensitivity and noise properties, in addition to components such as the X-ray tube, image intensifier and video camera. However, evaluations of the image-processing functions provided by DSA image processors have not been widely reported. This aspect of system evaluation is addressed Processing functions may be evaluated through densitometric comparisons of processed images with images generated by software techniques using real arithmetic. On the basis of such comparisons, the actual processing algorithms used in an image processor may be inferred Results for one system tested by this method indicate that processing functions are significantly at variance with the manufacturer's specification. Consequences for both processing and analysing DSA images and for acceptance-testing procedures of DSA systems are discussed.

DIGITAL SUBTRACTION ANGIOGRAPHY: A NEW METHOD FOR THE PHYSICAL ASSESSMENT OF IMAGING PERFORMANCE

N. E. Tomlinson, C. A. Greatorex and C. K. Battye

Department of Clinical Physics and Bioengineering, Guy's Hospital, London

A phantom and test object system has been devised for the rapid subjective and objective assessment of imaging performance obtained from modern commercially available DSA equipment. The test system is based upon the use of a variable depth water phantom which carries interchangeable test objects at a fixed depth with respect to the phantom input surface. The device measures the following image parameters, under conditions similar to those encountered in the clinical use of the imaging apparatus:

i) object contrast range accommodated within image data;
ii) minimum perceptible object contrast;
iii) minimum perceptible detail (contrast/spatial resolution);
iv) effective spatial resolution,
v) digital precision and dynamic range;
vi) minimum detectable iodine concentration,
vii) nature and extent of non-movement misregistration

In addition to descriptions of the principles, construction and use of the test system, results are also presented which demonstrate the imaging performance levels achieved by the four DSA systems tested to date. These are all cardiac capable, *i.e.* able to acquire data at a rate of 25 frames s^{-1} using a $512^2 \times 10$ matrix, state-of-the-art devices. Results are also given for modern cine-fluorographic imaging systems in order to allow comparison

Light Transmission

Chairman: Dr P. H. S. Smith

Transillumination—the characteristics and imaging properties of near infra-red radiation in tissue, by Mr H. Key, Mr J. Dykes, Dr B. L. Reece and Dr P. J. Roberts

The development of a system for computed transillumination tomography, by Dr P. C. Jackson, Mr J. M. Evans, Mr D. N. Ford, Mr D. Kear, Dr R. Skidmore, Mr J. H. Smith, Mr P. H. Stevens and Dr P. N. T. Wells

TRANSILLUMINATION: THE CHARACTERISTICS AND IMAGING PROPERTIES OF NEAR INFRA-RED RADIATION IN TISSUE

H. Key, J. Dykes, B. L. Reece and P. J. Roberts

Queen Elizabeth Medical Centre, Birmingham

In order that diagnostic imaging by transillumination may be developed, there is a need for greater understanding of the detailed transmission and scattering characteristics of visible and near infra-red radiation in tissue. This presentation is of measurements made in the near infra-red wavelength band 0.85–2.2 μm. Samples of blood at various haematocrits and dilutions in water, skeletal muscle, adipose tissue, liver, and bone have been studied. It was found that the spectral form is determined largely by the water and pigment content of the tissue, with recurring transmission peaks at about 1.1 μm, 1.3 μm and 1.6–1.7 μm. Evidence was obtained which suggested that large-angle scattering in blood and pigmented tissue falls with increasing wavelength. A phantom was designed to help in the choice of optimum laser wavelength for imaging.

THE DEVELOPMENT OF A SYSTEM FOR COMPUTED TRANSILLUMINATION TOMOGRAPHY

P. C. Jackson, J. M. Evans, D. N. Ford, D. Kear, R. Skidmore, J. H. Smith, P. H. Stevens and P. N. T. Wells

Department of Medical Physics, Bristol and Weston Health Authority

The use of transillumination to investigate the pathology of human organs (diaphanography) has enjoyed a revival in recent years, particularly in the study of breast lesions. The technique using video-acquisition and image-processing technology (tele-diaphanography), however, has yet to produce sensitivity and specificity that are comparable with the results obtained from mammography. An experimental computed transillumination tomography system has been designed and constructed for studying limbs, breast, testes and the neonatal head. Scans of phantoms demonstrating the spatial and contrast resolutions of the systems are shown and initial clinical results are presented

Instrumentation

Chairman: Dr P. H. S. Smith

Special collimators for quantitative imaging of high activity levels of ^{131}I, by Dr M. A. Flower, Dr I. Adam, Dr A. M. Masoomi and Dr T. Schlesinger

Dose reduction by rare-earth screens, by Dr H.-J. Maurer and F. Goos

Authomatic or manual exposure control in chest radiography? by Dr K. Faulkner, Mr M. D. H. Gordon, Mrs J. Miller and Miss M. Jones

A joint approach to quality control, by Miss J. Clark, Dr B. Heaton and Mr D. Davidson

SPECIAL COLLIMATORS FOR QUANTITATIVE IMAGING OF HIGH ACTIVITY LEVELS OF IODINE 131

M. A. Flower, I. Adam, A. M. Masoomi and T. Schlesinger

Physics Department, The Royal Marsden Hospital, Sutton, Surrey

High-resolution, low-sensitivity collimators have been made for a dual-headed whole-body scanner which was built originally for imaging low levels of radioactivity. The specifications were

(i) penetration and leakage effects to be minimised;
(ii) spatial resolution (in terms of full width at half maximum (FWHM) of line spread function) to be < 10 mm;
(iii) quantification of therapy levels of ^{131}I to be possible.

These specifications have been met as follows.

(i) The amount of lead surrounding the detectors has been increased to reduce penetration effects and all lead/lead interfaces were designed to minimise leakage effects
(ii) A nine-hole, 3 mm diameter, parallel-bore focused

collimator (focal length 200 mm) results in a FWHM of 8.0–9.8 mm within 200 mm Temex when isosensitive scanning is performed (counts from upper and lower detectors combined using geometric mean)

(iii) Quantitative imaging is achieved via isosensitive scanning. The calibration factor for these collimators is 12 counts/s per MBq/cm^2. Their sensitivity is such that a reading above background levels indicates the presence of a therapeutic amount of ^{131}I for carcinoma of the thyroid.

With much current interest in therapeutic applications of ^{131}I (*e.g.* antibodies and MIBG) and with the present inadequacies of rotating gamma cameras for high-energy single photon emission computed tomography, isosensitive scanning using dual-headed scanners and special collimators will have an important role to play.

DOSE REDUCTION BY RARE-EARTH SCREENS

H.-J. Maurer and F. Goos

Akademie Lehrkrankenhaus der Universität Heidelberg

Dose reduction with no loss of information is one of the main topics in X-ray diagnostics. We investigated some screen-film systems based on screens of different phosphors combined with varying film types. We used two groups of phosphors. (1) with a blue light emission spectrum with peaks in green ($CaWO_4$, LaOBr: Tb, Y_2O_2S: Tb) and (2) with a green light emission spectrum with only a few peaks in blue (Gd_2O_2S: Tb). Green sensitised films are necessary for Gd only.

All rare-earth screens show generally higher sensitivity and in general better spatial resolution than high speed calcium tungstate screens. X rays with rare-earth screens show more (La, Y) or less (Gd) structure (including noise), but without negative influence on analysis of details. The dose reduction, dependent on the rare-earth screen-film combination used, is by a factor of up to 10. Increasing speed of the systems causes decreasing spatial resolution.

AUTOMATIC OR MANUAL EXPOSURE CONTROL IN CHEST RADIOGRAPHY?

K. Faulkner, *M. D. H. Gordon, *J. Miller and †M. Jones

*Physics Department and †Medical Statistics Department, Christie Hospital and Holt Radium Institute, Manchester, and *X-ray Department, Burnley General Hospital*

The use of automatic and manual exposure control was investigated for a series of patients referred for chest radiography. All radiographs were taken using a postero-anterior projection in two rooms at the same general hospital. Each room was equipped with an air ionisation chamber type of automatic control. The effect of this equipment compared with manual exposure control on patient doses was investigated. Anterior and posterior radiation doses were measured using sachets of lithium fluoride. Detailed statistical analyses indicated that for each group of patients the anterior (exit) dose, and therefore all radiation dose, was lower using automatic control. The standard deviation on the anterior patient dose was lower under automatic control, which resulted in fewer repeat films due to incorrect density. Film densities were investigated to provide a further comparison between the two types of exposure control. Linear regression analysis of the radiation doses was performed. The results for the anterior doses indicated that the automatic exposure control adequately compensated for changes in tube potential and patient thickness. As anticipated, linear regression of the posterior doses revealed that doses were higher for both thicker patients and lower tube potentials.

A JOINT APPROACH TO QUALITY CONTROL

J. Clark, B. Heaton and D. Davidson

Department of Bio-Medical Physics and Bio-engineering, University of Aberdeen

The "X-ray quality assurance programme" currently being established in a joint project with the Department of Medical Physics, Aberdeen University and the Department of Diagnostic Radiology, Aberdeen Royal Infirmary is described. The aim of the project is a QA programme which (having been incorporated into the routine running of the department) is to be, for the most part, executed by radiographers and darkroom technicians with support from a medical physics department. The process of establishing the QA protocols is described with respect not only to system testing, but also to identifying those areas of QA for which responsibility lies with staff of the X-ray department and those for which Physicists can maintain responsibility. The role which X-ray service engineers can play in the implementation of such a programme is discussed. A summary of the progress made at 15 months into this joint project is given, including a description of record keeping facilities and analysis and interpretation of data, as well as an assessment of the effect of introducing such a programme.

Proceedings of The British Institute of Radiology

Vascular Radiology

Chairman: Professor E. Rhys Davies

The measurement of limb blood flow using Tc-labelled red cells, by Dr A. Parkin, Mr P A Wiggins, Dr P J. Robinson, Mr R. C. Kester, M. C. P. Salter and S. H. Leveson

Blood vessel imaging using ultrasound techniques, by Dr K. N. Humphries, V. Gazzard, Dr T. K. Hames and Dr A Chant

Accuracy and errors of non-invasive measurements of blood flow by Doppler ultrasound, by Dr M. I Qamar, J. Beard, J. Evans, R. Skidmore, Dr P N. T. Wells and A. E. Read

Combined real-time B-scan haemodynamic flow imaging—a review, by Dr K N Humphries, Dr T. K. Hames and Dr T. Wilmhurst

Assessment of pulsatility index in the diagnosis of carotid artery disease, by Mr M I. Aldoori, Dr R. E. Lee, Dr C E. Francis and Mr R. N Baird

The role of the Vascular Studies Unit in assessing the outcome of percutaneous transluminal angioplasty in the lower limb, by Miss S E. A Cole, Dr W. D. Jeans, Mr M. Horrocks and Mr R. N. Baird

Duplex scanning in the evaluation of carotid bruit: Mr M I. Aldoori, Dr G. L. Benviste, Dr J. Fairgrieve and Mr R N. Baird

Dynamic CT scanning of inflammatory aortic aneurysms, by Dr P. M. Taylor and Dr J. E. Adams

Biochemical changes following balloon dilatation of iliac artery stenosis in atherosclerotic patients, by Dr C J. Garvey, R. A. Wilkins, M. A. Bettman, S. Coade and J. Gordon

Low-dose intra-arterial streptokinase therapy—results, risks and points of technique, by Dr W. J Walker, Mr A E. B. Giddings and Dr A. J. Thompson

Takayasu's arteritis, by Dr M. Yamoto, Dr J. Lecky, Dr K. Hiramatsu and Dr E. Kohda

THE MEASUREMENT OF LIMB BLOOD FLOW USING TECHNETIUM-LABELLED RED CELLS

A. Parkin, P. A. Wiggins, *P. J. Robinson, †R. C. Kester, †M. C. P. Salter and ‡S. H Leveson

*Departments of Medical Physics, *Diagnostic Imaging and †General Surgery, St James's University Hospital, Leeds, ‡Department of General Surgery, York District Hospital*

A method for measuring below-knee blood flow during reactive hyperaemia has been developed Subjects are positioned with legs and feet within the field of view of a gamma camera and pneumatic cuffs are placed below the knees to isolate the blood and induce a hyperaemic response The remaining blood pool is labelled with technetium-labelled red cells. Blood flow is derived from the initial gradient of a time–activity curve generated for the lower leg following release of the cuff and from equilibrium blood sampling. A tissue-equivalent phantom of a human leg connected to a peristaltic pump has been used to validate the technique and good agreement has been observed between measured flow rates and those calculated from time–activity curves ($r = 0.99$) The method has been applied to patients with peripheral vascular disease and to normal controls The mean value (±SD) of limb perfusion for normal controls (24 limbs) was found to be 15 6±3 5 ml/100 ml/min and for patients with intermittent claudication (14 limbs) was 4.6±2.0 ml/100 ml/min. Flow measurements are found to correlate with clinical findings and with symptoms Reproducibility, established by repeated measurements on 16 limbs, is high ($r = 0\ 96$) The method is well tolerated, even by patients suffering from rest pain.

BLOOD VESSEL IMAGING USING ULTRASOUND TECHNIQUES

K. N. Humphries, V. Gazzard, T. K. Hames and A. Chant

Vascular Group, Medical Physics and Surgery Departments Southampton General Hospital

A number of studies are in progress to investigate the potential of duplex scanning for the detection of occlusive and aneurysmal disease in the extracranial and lower limb arteries and for longitudinal monitoring of vessel patency following endarterectomy and bypass operations. Groups of patients with symptomatic peripheral vascular disease undergoing either aortography or angiography and patients who have had either carotid endarterectomy or lower limb bypass operations, have been examined using the duplex technique For the extracranial examination, images have been obtained of the common carotid from the base of the neck and the internal and external carotid arteries to the level of the jaw For the abdominal and lower limb studies, emphasis has been placed on obtaining images of the distal aorta, common femoral bifurcation and the popliteal bifurcation. In a number of these patients, direct scanning along the main arteries of the lower limb arterial tree has been attempted A categorisation of any disease present was made on the basis of the Doppler information, including waveform signature changes, the presence of turbulence and increases in frequency shift, and the presence of echogenic areas within the vessel lumen as displayed on the B-scan image.

The preliminary results of this technique, when compared with arteriography, show sensitivities and specificities of > 90% in the differentiation of disease causing greater than or less than 50% lumen constriction A discussion of the accuracy of this technique in detecting early disease is also presented. In conclusion, these studies indicate that duplex scanning is a powerful investigative tool which has a major role to play in the non-invasive assessment of the peripheral vasculature In addition, this technique has the potential to replace conventional arteriography in specific situations

ACCURACY AND ERRORS OF NON-INVASIVE MEASUREMENTS OF BLOOD FLOW BY DOPPLER ULTRASOUND

M. I. Qamar, J. Beard, J. Evans, R. Skidmore, P. N. T. Wells and A. E. Read

Departments of Medicine, Surgery and Medical Physics, Bristol Royal Infirmary

Non-invasive measurement of blood flow in the major gastrointestinal arteries in man, using a duplex scanner (ATL 500), has been introduced recently (Qamar et al, 1985). The aim of the present study was to assess the *in vitro* accuracy of the method and its errors

In vitro calibration of the method was carried out using a hydraulic system under conditions simulating superior mesenteric artery flow in humans and allowing simultaneous comparative Doppler ultrasound and electromagnetic measurements flow in a latex tube Comparative flow measurements (Doppler ultrasound vs electromagnetic method) were performed for flows of 150 ml/min to 1000 ml/min. The coefficient of correlation (r) was 0 98; the slope of regression was 1 008 with an intercept of 15 9 ml/min. Measurements by Doppler ultrasound slightly overestimated flow and the error average was 4% In a second experiment, the effect of incomplete insonation of the latex tube was assessed. The experiment was carried out in exactly the same way as above but the diameter of the latex tube was calibrated directly and considered for the calculation of blood flow The flow measured by Doppler ultrasound was overestimated by an average of 50% when compared with the electromagnetic recordings The error ranged from 45% to 65% In a third experiment, latex tubes of calibrated internal diameter which varied from 3 mm to 12 mm were measured from the real-time imaging system while immersed 7 cm below the surface of a water bath This was a double-blind experiment in which 40 comparative measurements were performed All measurements from the real-time imaging were less than the actual values by 1 mm

In conclusion, the method has two systematic errors: the incomplete insonation (which leads to overestimation in flow) and the underestimation of diameter, which largely offset each other so that the resulting measurement of blood flow has an acceptable accuracy.

REFERENCE

QAMAR, M I, READ, A. E, SKIDMORE, R., EVANS, J M & WELLS, P. N T, 1985. Gastrointestinal blood flow in man determined by Doppler ultrasound technique. In *WFUMB 85, Proceedings of the Fourth Meeting of the World Federation for Ultrasound in Medicine and Biology and the First World Congress of Sonographers, Sydney, Australia.* Ed. by R W. Gill & M J Dadd (Pergamon Press, London, New York), p 164.

COMBINED REAL-TIME B-SCAN AND HAEMODYNAMIC FLOW IMAGING: A REVIEW

K. N. Humphries, T. K. Hames and T. Wilmhurst

Department of Medical Physics, Southampton General Hospital

The introduction of duplex scanning during the last decade has given considerable impetus to the non-invasive assessment of both peripheral and abdominal blood vessels and cardiac function The first-generation systems have used combined real-time B-scan and single-gate pulsed Doppler information However, with the introduction of serial data processing techniques, combined real-time B-scan/flow imaging systems have been developed which are capable of assessing blood velocities at any point within the sector scan. The anatomical information is displayed in shades of grey and the velocity information is colour coded with shades of red and orange representing flow in one direction, and shades of blue and green showing areas of flow in the opposite direction A description of the basic principles involved will be presented and examples of peripheral vessel and cardiac images in normal and diseased conditions are shown The potential of these techniques in replacing arteriography will also be discussed.

ASSESSMENT OF PULSATILITY INDEX IN THE DIAGNOSIS OF CAROTID ARTERY DISEASE

M. I. Aldoori, R. E. Lee, *C. E. Francis and R N. Baird

*Department of Surgery and *Department of Medical Physics, Bristol Royal Infirmary*

Duplex scanning is well established in the non-invasive diagnosis of carotid stenosis and shows excellent correlation with radiological assessment (Langlois et al, 1983) This relatively expensive technique is, however, available in only a few centres, and a need exists for a more available reliable test.

A prospective study has been undertaken in 25 patients using a simple bidirectional 10 MHz continuous Doppler system to record signals from the common carotid artery and from the supratrochlear artery in order to assess the value of the pulsatility index (PI) in the diagnosis of internal carotid artery stenosis. Pulsatility indices were calculated from signals obtained from both arteries and expressed as a ratio of PI (supratrochlear)/PI (common carotid) This ratio was correlated with percentage stenosis measured from triplanar cerebral angiography Using the PI ratio there was almost complete separation of values associated with > 70% stenosis or complete occlusion from lesion at < 70% ($P = < 0.002$, Mann-Whitney).

The PI ratio is an inexpensive and reliable test requiring much less expertise and equipment than duplex scanning It could be useful in centres which do not have easy access to a duplex scanner

REFERENCE

LANGLOIS, Y., ROEDERER, G. O, CHAN, A et al, 1983. Evaluation carotid artery disease The concordance between pulsed Doppler/spectrum analysis and angiography *Ultrasound in Medicine & Biology, 9*, 51–63

THE ROLE OF THE VASCULAR STUDIES UNIT IN ASSESSING THE OUTCOME OF PERCUTANEOUS TRANSLUMINAL ANGIOPLASTY IN THE LOWER LIMB

S. E A Cole, W. D. Jeans, M Horrocks and R. N. Baird

Department of Radiodiagnosis, Bristol Royal Infirmary

Since the very first use of PTA in this hospital as a means of treating arterial disease in the lower limb, the Vascular Studies Unit has been committed to monitoring patients after Gruntzig dilatation Two broad aims have been identified

1 To monitor patients closely and objectively in order to make an early assessment of failure so as to facilitate early correction.
2 To assess the long term efficacy of PTA

The various methods of assessment of the Unit are described The difficulties in classifying the results and the ground rules for deciding between failure and success are discussed One of the main points already emerging is the need to judge the result for claudicants and limb-salvage patients by different criteria. It is shown that a very simple test such as Doppler ankle pressure has a very useful predictive value for long-term patency, and the effects of continued smoking after PTA are discussed A very brief outline of the results of our 310 Gruntzig dilatations is given

DUPLEX SCANNING IN THE EVALUATION OF CAROTID BRUIT

M. I. Aldoon, G. L. Benveniste, *J. Fairgrieve and R. N. Baird

*Department of Surgery, Bristol Royal Infirmary and *Cheltenham General Hospital*

Sixty-one patients presenting for duplex ultrasound assessment of asymptomatic cervical bruit between September 1980 and September 1983 were reviewed in 1985 to assess progression of disease, and current clinical status. The mean follow-up period was 33 (range 24–60) months. There were 12 deaths in the group; six were due to stroke, eight to myocardial infarction and three to malignant disease. One patient suffered a non-fatal stroke.

On the basis of the original scan (and arteriography if available), the patients were divided into five groups (A–E) based on the severity of internal carotid artery stenosis: A, normal, B, <50%; C, 50%–75%; D, >75%, and E, occlusion. Mortality rates per group were A, 0% (0/5), B, 23% (7/30), C, 29% (2/7), D, 50% (3/6), and E 43% (3/7). There were, however, no stroke related deaths in the first three groups (*i.e.* less than 75% stenosis). In those patients with greater than 75% stenosis or occlusion, 30% died due to stroke ($P = 0.001$, Fisher's exact test).

We conclude from our study that patients with asymptomatic carotid bruit should be investigated, as those with severe disease have a high risk of death from stroke.

DYNAMIC COMPUTED TOMOGRAPHIC SCANNING OF INFLAMMATORY AORTIC ANEURYSMS

P. M. Taylor and J. E. Adams

Department of Diagnostic Radiology, University of Manchester

Approximately 20% of abdominal aortic aneurysms are of the inflammatory type (Bloor & Humphries, 1979). In the variant, the aneurysm is surrounded by a "cuff", the histological composition of which is similar to that found in retroperitoneal fibrosis. The term "periaortitis" has been suggested to encompass both lesions (Dixon et al, 1984). This inflammatory tissue poses problems for the surgeon at operation, and consequently these patients are frequently treated with a course of oral steroids prior to surgical treatment.

Eight patients with inflammatory aortic aneurysm have been scanned using a GE 8800 scanner. Each patient was scanned before intravenous contrast-medium administration, and then a dynamic series of sections was obtained during the infusion of 100 ml Conray 280 (meglumine iothalamate). In addition to demonstrating the size of the aneurysm and the extent of the surrounding soft-tissue mass, dynamic CT showed enhancement of the inflammatory "cuff" in all cases. The attenuation values of the inflammatory mass increased by 29.6 HU (mean) from the pre-contrast values of 30–50 HU (mean 39.8 HU). Four patients were treated with steroids and rescanned. In each case there was a reduction in size and degree of contrast enhancement of the periaortic soft-tissue mass. Thus dynamic CT is useful in the diagnosis of inflammatory aortic aneurysms and in monitoring the response to steroid therapy. This has implications for surgical management.

REFERENCES

BLOOR, K. & HUMPHRIES, W. V., 1979. Aneurysms of the abdominal aorta. *British Journal of Hospital Medicine, 21,* 568–583.

DIXON, A. K., MITCHINSON, M. J. & SHERWOOD, T., 1984. Computed tomographic observation in periaortitis: a hypothesis. *Clinical Radiology, 35,* 39–42.

BIOCHEMICAL CHANGES FOLLOWING BALLOON DILATATION OF ILIAC ARTERY STENOSIS IN ATHEROSCLEROTIC PATIENTS

C. J. Garvey, R. A. Wilkins, M. A. Bettman, S. Coade and J. Gordon

Departments of Radiology and Vascular Biology, Northwick Park Hospital and Clinical Research Centre, Harrow, Middlesex

In an attempt to define the biochemical changes resulting from balloon angioplasty, nine patients with atherosclerotic stenosis of the iliac arteries were studied. Using the balloon catheter and a side-arm sheath as sampling catheters, it was possible to obtain blood samples directly from the artery above and below the angioplasty site, before and after balloon dilatation. Serial venous samples were also obtained in a number of patients. Blood was collected directly into an anticoagulant cocktail and the plasma separated and stored. Plasma was subsequently analysed using radioimmunoassay techniques and high pressure liquid chromatography (HPLC) for a variety of markers of endothelial cell damage, platelet and complement activation. These included prostacyclin, nucleotides and nucleosides, thromboxane, and C3A and C5A release. This study showed that there were no significant changes in any of the parameters measured. The implications of these findings and the relevance to clinical follow-up in these patients are discussed.

LOW-DOSE INTRA-ARTERIAL STREPTOKINASE THERAPY: RESULTS, RISKS AND POINTS OF TECHNIQUE

W. J. Walker, A. E. B. Giddings and A. J. Thompson

Royal Surrey County Hospital, Guildford

By the end of July 1985, 28 patients with acute or subacute peripheral arterial ischemia were treated with low-dose intra-arterial streptokinase as part of an ongoing trial to assess the benefits of the procedure compared to its risks. In over 60% of patients complete lysis was obtained for a major complication rate of 11% including one mortality. Up to 3-year follow-up was obtained. From the results it is concluded that thrombolysis is superior to surgery for the treatment of these patients. Updated results are presented and the following important aspects discussed:

(1) use of small, *e.g.* 5 French, catheters,
(2) approach from the contralateral groin;
(3) incidence and treatment of retrograde thrombosis;
(4) necessity of urgent treatment of revealed cause of occlusion,
(5) technique for conversion to heparin and withdrawal of catheter at end of procedure,
(6) effect of low-dose therapy on clotting profile,
(7) rationale for initial 12–14 h trial of streptokinase therapy to reduce complication rate.

TAKAYASU'S ARTERITIS

M. Yamoto, J. Lecky, K. Hiramatsu and E. Kohda

School of Medicine, University of Pittsburgh, Pennsylvania, USA

Fifty-nine cases of Takayasu's arteritis were retrospectively analysed. On chest radiography ($n = 49$), 68% of the cases showed abnormalities with irregular contour of the descending aorta being the most common finding (67%), followed by calcification in the arch and the descending aorta (27%), and ectatic aortic arch (27%). Fifty cases of total aortography were categorised into four types according to Nasu's classification. The extensive type (type 4) was 68%, and 28% of the cases consist of the classical "pulseless disease" type (types 1 and 2). Among the changes in the aorta, stenosis was the most common finding (71%), followed by thickening of the wall (67%), contour irregularity (37%), tortuosity (34%) and dilatation (24%). Occlusion, aneurysm and aortic regurgitation were seen in a small number of patients. Dissecting aneurysm, a rare manifestation, was seen in one case. The adventitial vascular structure, the vasa vasorum was seen in the wall of the proximal descending aorta in three cases and the aetiologies were speculated. In branches of the aorta, stenosis was the most common finding, involving most commonly, aortic arch branches. On pulmonary arteriography (n = 21) 86% were abnormal with occlusive change being the most common finding. No predilection for any lobe was noted.

Genito-urinary Radiology

Chairman: Dr P. Davies

Prospective analysis of a new contrast-clearance method for the determination of glomerular filtration rate, by Dr A. J. Pollard, P. H. O'Reilly, Dr P. J. Martin, P. J. C. Brooman, G. G. Mason and N. B. Farah

Adrenal calcifications, by Dr J. W. Lecky, Dr R. J. Penkrot, Dr C. R. Fuhrman and Dr M. Yamoto

Renal size, papillary blush and contrast osmolality in intravenous urography, by Dr R. Whitehouse

Dehydration, antidiuretic hormone and the intravenous urogram, by Dr M. Trewhella, Dr M. Forsling, Dr D. Rickards and Dr P. Dawson

Influence of contrast-medium dose and other factors in excretion urography, by Dr C. F. Loughran, G. Ansell, C. R. West and M. Learmonth

The intravenous urogram in prostatism—is it necessary? By Dr S. Johnson, Dr G. de Lacey and Dr B. Twomey

Adrenal and genitourinary lymphoma—radiological and pathological correlations, by Dr J. W. Lecky, R. P. Wiley and T. Talamo

Diabetes mellitus and the genito-urinary tract, by Dr J. W. Lecky, C. R. Jarmolowski, F. J. Simone and R. L. Myerwitz

Videocystourethrography in children, by Miss H. Fitzmaurice and Dr D. Rickards

Barium double-contrast cystography, by Dr J. R. Harding

Ultrasound of the urethra in post-prostatectomy incontinence, by Dr D. Rickards, Dr H. Fitzmaurice and Dr M. A. Hall-Craggs

Radiological changes in the lower urinary tract after radiotherapy for carcinoma of the uterine cervix, by Dr P. M. Taylor, Dr R. J. Johnson and Dr B. Eddleston

PROSPECTIVE ANALYSIS OF A NEW CONTRAST-CLEARANCE METHOD FOR THE DETERMINATION OF GLOMERULAR FILTRATION RATE

A. J. Pollard, P. H. O'Reilly, P. J. Martin, P. J. C. Brooman, G. C. Mason and N. B. Farah

Departments of Radiology, Urology and Biochemistry, Stepping Hill Hospital, Stockport, Cheshire

A new method for the derivation of glomerular filtration rate which depends on the measurement of plasma disappearance of intravenous contrast media was investigated. The method is based on X-ray fluorescence of iodine. The equipment incorporates two americium-241 sources, each emitting directionally controlled 60 keV photons. Iodine atoms in post-urography plasma samples subjected to this gamma radiation emit characteristic X rays in proportion to the iodine concentration. These are monitored by a NaI detector and six-channel analyser/microcomputer (Elementanalysis ab, Sweden) to calculate the glomerular filtration rate.

Eighty-seven patients attending the urological unit were investigated. 54 patients had simultaneous clearance studies using ^{51}Cr-EDTA and 100 ml iohexol (Omnipaque; Nyegaard) and 33 had the same procedure using 50 ml iohexol. In 33 cases, simultaneous endogenous creatinine clearances were performed. Ten contrast specimens were subsequently frozen and re-examined at weekly intervals for 6 weeks. Correlation between ^{51}Cr-EDTA clearance and contrast clearance using 100 ml iohexol, was excellent ($r = 0.90$) and, using 50 ml iohexol, was very good ($r = 0.85$). Correlation between ^{51}Cr-EDTA and creatinine clearance was less impressive ($r = 0.69$). The reproducibility of the contrast clearance method was excellent, with no significant statistical variation over 60 examinations during 6 weeks. The technique is simple to perform, can be used as an adjunct to urography and can be repeated for serial studies.

ADRENAL CALCIFICATIONS

J. W. Lecky, R. J. Penkrot, C. R. Fuhrman and M. Yamoto

University of Pittsburgh, Pennsylvania, USA

Adrenal calcifications may be clinically divided into those lesions commonly seen in the newborn or children and those seen in the adult. In childhood, adrenal cystic disease (predominantly neonatal haemorrhage) and neuroblastoma are quite common. In adulthood, cystic disease, carcinoma, adenoma and phaeochromocytoma are common. The various types of calcifications seen in these lesions will be presented.

In general, ultrasound is not indicated in the investigation of calcified adrenal lesions because of the problem of acoustical reverberation. Computed tomography is the method of choice in most instances. The need for angiography has been drastically curtailed. With the availability of percutaneous needle biopsy, surgery in malignant diseases with computed tomographic evidence of extension is subject to reappraisal.

Representative examples with varying calcified patterns will be presented. The use of adrenal biopsy will be discussed.

RENAL SIZE, PAPILLARY BLUSH AND CONTRAST OSMOLALITY IN INTRAVENOUS UROGRAPHY

R. Whitehouse

Department of Diagnostic Radiology, University of Manchester

A papillary blush, due to contrast medium visible in the collecting tubules, occurs in 1% of normal urograms performed with conventional ionic contrast agents (Palubinskas, 1963). Within 30 s of contrast medium injection, most kidneys swell by 10–20% in volume (Dorph et al, 1977). In view of the reduced osmolality and increase in urinary iodine concentration achieved with non-ionic contrast agents, the incidence of papillary blush and changes in renal length were assessed in a randomised single-blind prospective study of 57 patients receiving 50 ml of either Na : Mg diatrizoate (Urografin 370) or iohexol (Omnipaque 350). The mean increase in renal length of 3.5 mm between the control and 5 min film confirms previous studies of ionic contrast agents and was not significantly different for the two contrast agents. Papillary blush occurred in one patient (3%) receiving Urografin but in 14 (47%) patients receiving Omnipaque. Although it has long been recognised that a papillary blush is a normal finding at intravenous urography, a similar appearance can occur in medullary sponge kidney and early papillary necrosis. With the increasing use of non-ionic contrast agents, an awareness of the common occurrence of a papillary blush should be recognised and not misinterpreted as pathological.

REFERENCES

DORPH, S., SOVAK, M., TALNER, L. B. & ROSEN, L., 1977. Why does kidney size change during intravenous urography? *Investigative Radiology, 12*, 246–250.

PALUBINSKAS, A. J., 1963. Renal pyramidal structure opacification in excretory urography and its relation to medullary sponge kidney. *Radiology, 81*, 963–970.

DEHYDRATION, ANTIDIURETIC HORMONE AND THE INTRAVENOUS UROGRAM

M. Trewhella, *M. Forsling, †D. Rickards and ‡P. Dawson

*Department of Radiology, Princess Mary Royal Air Force Hospital, Halton, †Departments of Radiology and *Physiology, Middlesex Hospital, London and ‡Royal Postgraduate Medical School, Hammersmith Hospital, London*

Dehydration prior to intravenous urography has been advocated since the 1930s, the theoretical basis of it being that by elevating vasopressin levels, water reabsorption in the distal and collecting tubules of the kidney is enhanced, increasing the urinary concentration of contrast medium. In recent years the effectiveness of dehydration in improving diagnostic image quality has been questioned. It was decided to determine vasopressin levels in patients who had been routinely dehydrated prior to intravenous urography both before and following administration of contrast medium. The results show that not only do the traditionally practised regimes of dehydration fail to raise vasopressin levels, but also that the administration of contrast medium itself causes a rapid and profound rise in vasopressin levels which prevail while films showing pyelographic detail are being taken. As it is the administration of contrast medium which results in the prevailing elevated vasopressin levels rather than the preceding dehydration, we conclude that the degree of dehydration routinely undertaken is irrelevant to image quality. It cannot, therefore, be justified, particularly in view of current understanding of its possible role in contrast-medium induced renal impairment in risk groups such as diabetics and the elderly.

INFLUENCE OF CONTRAST-MEDIUM DOSE AND OTHER FACTORS IN EXCRETION UROGRAPHY

*†C. F. Loughran, *G. Ansell, ‡C. R. West and *M. Learmonth

**Department of Radiology, Whiston Hospital, Prescot, Merseyside and the Department of Radiodiagnosis, University of Liverpool, †Department of Radiology, Medical University of South Carolina, Charleston, South Carolina, USA, ‡Biostatics Unit, Department of Medicine, University of Liverpool*

To investigate the wide diversity of contrast-medium dose for excretory urography noted in a previous survey (Ansell et al, 1980), 1008 urograms from 14 hospitals within the UK were reviewed after a period of 5 years and the results subjected to computer analysis. The hospitals which employed differing contrast-medium doses were divided into five dose ranges: (1) 14 g I or less, (2) 14–18 g I, (3) 20–23 g I, (4) 24–27.5 g I, and (5) 29 g I or more.

In general, there was a positive association between the confidence with which the urograms could be interpreted and the dose of contrast medium. There was no evident value in using doses in excess of 27 g I except in older patients. Age was an important factor in urographic quality. In young patients (20 years or less), diagnostic urography was obtained in 93.4% of all cases and there was no demonstrable benefit in increasing the dose above that used in Group 1 (14 g I or less). When the patient was aged 70 years or more, a dose in excess of 29 g I obtained diagnostic urograms in 75.5% of patients. Higher contrast-medium doses did not effect a reduction in film usage. Increasing the amount of radiographic film used did have a favourable influence on diagnostic accuracy and this effect operated independently of contrast-medium dose. The value of compression in urography was confirmed. Insofar as it was possible to assess, diagnostic accuracy was generally high, with the exception of bladder tumour diagnosis where approximately one-third of cases were undetected at the initial urogram. There is a case for reconsideration of contrast-medium doses and techniques currently used in excretory urography.

REFERENCE

ANSELL, G., TWEEDIE, M. C. K., WEST, C. R., PRICE-EVANS, D. A. & COUCH, L., 1980. The current status of reactions to intravenous contrast media. *Investigative Radiology, 15* (Suppl.), S32–S39.

THE INTRAVENOUS UROGRAM IN PROSTATISM: IS IT NECESSARY?

S. Johnson, G. de Lacey and B. Twomey

Department of Radiology, Northwick Park Hospital and Clinical Research Centre, Harrow

We present the results of a prospective survey of the effect on management of a routine IVU on patients referred with prostatic symptoms but without a history of acute retention, haematuria, or previous known renal disease. One hundred and ten consecutive patients with prostatic symptoms and referred to the urology outpatients department were included in the survey. Prior to requesting an IVU, the urologist completed a stamped questionnaire of the patient's symptoms, his diagnosis, and most importantly his proposed (pre-IVU) management. A standardised IVU and an ultrasound scan of the kidneys, bladder and prostate were performed within a week of each other. The IVU was assessed by a consultant radiologist. The clinical notes of all patients were subsequently studied to determine the eventual post-IVU management of each patient, and the influence of the IVU and/or ultrasound findings on the urologist's original planned management.

Of 110 consecutive patients, 104 were included in the final analysis, six patients being excluded because their investigations were incomplete. Several results from this survey are presented. The principle conclusion is that neither the IVU nor ultrasound altered clinical management in any patient, and that neither investigation is essential in patients with prostatic symptoms. The potential financial saving to the NHS of excluding an IVU as a routine is assessed.

ADRENAL AND GENITOURINARY LYMPHOMA RADIOLOGICAL AND PATHOLOGICAL CORRELATIONS

J. W. Lecky, R. P. Wiley and T. Talamo

University of Pittsburgh, Pennsylvania, USA

Lymphomatous involvement of the genitourinary tract usually manifests itself as multiple small nodules involving both kidneys with or without lymph-node involvement producing deviation of one or both ureters. This type of renal involvement, along with the diffuse tumour infiltration, most frequently produces renal enlargement without evidence of intrarenal masses. On other occasions, solitary renal masses are visible on the urogram and less commonly renal displacement, renal vascular involvement, alterations in renal physiology secondary to tumour infiltration or medial deviation of the ureters are seen. Lymphomatous involvement of the bladder area usually occurs with approximately one-third of the frequency of renal involvement with extrinsic displacement and/or invasion of the bladder wall by adjacent pelvic masses. This occurs more frequently than intrinsic bladder lymphoma.

We present information from more than 35 cases demonstrating the more uncommon urographic, ultrasonic, computed tomographic, angiographic and pathological manifestations of genitourinary and adrenal lymphoma.

The case material includes adrenal lymphomatous masses (unilateral and bilateral), adrenal encasement, renal lymphoma producing hypertension with resolution after treatment, juxtarenal involvement producing renal-vein occlusion and encasement of the renal pelvis, unilateral solitary renal masses, bilateral renal displacement, diffuse bilateral renal enlargement secondary to infiltration with and without associated calyceal obliterations, various patterns of ureteral displacement and encasement and lymphomatous bladder involvement (both extrinsic and intrinsic).

DIABETES MELLITUS AND THE GENITOURINARY TRACT

J. W. Lecky, C. R. Jarmolowski, F. J. Simone and R. L. Myerwitz

University of Pittsburgh, Pennsylvania, USA

The urinary tract of the diabetic is susceptible to an array of pathological entities which can be observed and frequently definitely diagnosed on the plain radiograph, intravenous or retrograde pyelogram with occasional assistance from other imaging modalities.

Inappropriate vascular calcification of the medial type, particularly in the hypogastric aorta and renal artery in young males or females, vas deferens calcification and renal enlargement strongly suggest diabetes. Diabetes mellitus is the most common identifiable cause for renal enlargement in our institution.

Emphysematous nephritis, perinephritis, cystitis and urogenic bladder, chronic pyelonephritis, renal abscess, xanthogranulomatous pyelonephritis, renal medullary necrosis and primary renal and bladder candidiases are also recognised complications. Representative radiographical and pathological correlations are presented.

VIDEOCYSTOURETHROGRAPHY IN CHILDREN

H. Fitzmaurice and D. Rickards

Department of Imaging, Middlesex Hospital, London

Videocystourethrography (VCUG) combines imaging of the lower urinary tract with pressure measurements giving anatomical and functional information. It is a well established technique in adults, but its role in the investigation of children with disturbances of micturition is less clear.

Twenty incontinent boys age 3–16 years have been studied using VCUG. All the boys had undergone surgery for posterior urethral valves. In every case, a urodynamic abnormality was identified by VCUG. The commonest urodynamic abnormality was detrusor instability which did respond to treatment in most cases. No evidence of distal urethral sphincter weakness was found. High pressure detrusor instability was seen in four boys with chronic renal failure.

We conclude that VCUG is an important technique for diagnosis in this group of patients and helps to identify appropriate treatment selection. The technique also helps to demonstrate the relationship between bladder behaviour and kidney function.

BARIUM DOUBLE-CONTRAST CYSTOGRAPHY

J. R. Harding

St Woolos Hospital, Newport, Gwent

The use of sterile barium for cystography fell out of practice a decade or more ago, mainly because of complications when reflux occurred in paediatric patients. Improvements in mucosal imaging in the gastrointestinal tract by the double-contrast technique, following the development of modern high-density barium preparations along with better image resolution due to improvement in radiographic equipment, film and intensifying screens, have stimulated this preliminary study in the investigation of suspected bladder tumours. Thirty-eight double-contrast cystograms have been performed in 50 patients, after first excluding reflux with a water-soluble cystogram, providing excellent visualisation of neoplasm with 100% true positive and true negative rates when compared with cystoscopy and histology, there were no false negative examinations and one false positive examination was due to a ureterocele. It is possible to assess accurately the presence or absence of bladder neoplasms, along with details of their number, exact site, size and shape, and whether polypoid or not, this has proved to be useful pre-cystoscopic information. The technique has been helpful where cystoscopy has been difficult or impossible, and also for looking for neoplasm within bladder diverticula. In summary the technique is highly sensitive and specific, and can provide high quality images for diagnostic purposes

ULTRASOUND OF THE URETHRA IN POST-PROSTATECTOMY INCONTINENCE

D. Rickards, H. Fitzmaurice and M A. Hall-Craggs

Department of Imaging, The Middlesex Hospital, London

Trans-urethral resection of the prostate (TURP) necessitates obliteration of the bladder neck mechanism Continence then depends on the distal sphincter mechanism alone. Incontinence following TURP may be due either to bladder instability or to weakness of the distal sphincter mechanism or a combination of the two. Twenty patients with post-prostatectomy incontinence have been studied with both linear-array transrectal ultrasound of the urethra and videocystourethrography (VCUG) In 10 cases, incontinence was due to bladder instability Ultrasound in all 10 demonstrated the TURP cavity and was able to demonstrate good distal sphincter closure during interruption of micturition, findings confirmed by VCUG Ultrasound had no role to play in assessing bladder function itself In the other 10 patients, incontinence was due to a deficient distal sphincter mechanism Again, ultrasound was able to image the failure of the distal sphincter to close sufficiently to interrupt micturition, findings again confirmed by VCUG

We conclude that linear-array transrectal imaging of the urethra is a promising non-invasive primary technique to investigate patients with post-prostatectomy incontinence.

RADIOLOGICAL CHANGES IN THE LOWER URINARY TRACT AFTER RADIOTHERAPY FOR CARCINOMA OF THE UTERINE CERVIX

P M. Taylor, *R. J. Johnson and B. Eddleston

*Department of Diagnostic Radiology and *Christie Hospital and Holt Radium Institute, University of Manchester*

Radiotherapy for carcinoma of the cervix inevitably results in irradiation of the adjacent ureters and bladder In order to attempt to identify the radiological criteria which may enable a positive diagnosis of radiotherapy change as opposed to recurrent local disease, the radiographs of 36 patients with proven radiation-induced abnormalities were reviewed Within this group there was a high incidence of ureteric abnormalities previous studies had suggested that ureteric damage is rare (Slater & Fletcher, 1971). The commonest lesion is a smooth stricture at the vesico-ureteric junction, although strictures were also found in the more proximal ureter There was a high level of associated bladder abnormalities, 21 patients having both ureteric and vesical lesions. The principal abnormal findings in the bladder were disruption of the mucosal pattern, thickening of the bladder wall and fistula formation. Changes were noted in patients receiving intracavitary treatment. external radiotherapy and the two in combination The abnormalities were usually readily seen on the intravenous urogram, but both ultrasound and CT scanning were seen to demonstrate some lesions more effectively

REFERENCE

SLATER, J M. & FLETCHER, J. H , 1971. Ureteral strictures after radiation therapy for carcinoma of the uterine cervix *American Journal of Roentgenology, 111*, 269–272

Radiotherapy and Oncology

Chairman: Dr D. Pearson

Rectal complications after pion treatment at the Swiss Institute for Nuclear Research, by Dr K. O. Matsumoto, Dr R. Greiner, Dr H. Blattmann and Dr P. Thum

The relationship of the bladder and the cervix in patients undergoing intracavitary therapy, by Dr H R. Lukka, C. J. Moore and R. D. Hunter

Contact therapy of tumour recurrences in the regions of the pharynx and oral cavity by means of a remote-controlled afterloading technique, by Dr M. Bauer, Dr R. Schulz-Wendtland, Dr H. Kuttig and Dr P. Fritz

How should we manage glomus jugulare tumours in 1986? by Dr P. J. D. K. Dawes, Dr C. C. Gaffney and Dr G. Lambert

Intrathecal targeted therapy for neoplastic meningitis with radiolabelled monoclonal antibodies—a report of three cases, by Mr H B. Coakham, Dr R. B. Richardson, Dr A. G Davies, Dr S P. Bourne, Dr D H. Jones and Dr J T Kemshead

Complications and 5-year results of treatment of carcinoma of the cervix using the Cathetron in rural India, by Professor V. Balasundaram, Dr K Koteshwer Rao and Mr J. G. R Solomon

The study of zinc in oncology, by Dr L. Grant

Vaginal packing, by Dr E Dvořák and Dr S. Song

RECTAL COMPLICATIONS AFTER PION TREATMENT AT THE SWISS INSTITUTE FOR NUCLEAR RESEARCH

K. Matsumoto, R. Greiner, H Blattmann and P. Thum

Medical Project, Swiss Institute for Nuclear Research, Villigen, Switzerland

Since December 1981 it has been possible to carry out conformal, dynamic, microprocessor-controlled radiotherapy of deep-seated tumours with negative pions in the Piotron at the Swiss Institute for Nuclear Research (SIN) The chosen method was "spot scan", whereby the patient is moved in three dimensions relative to a beam spot a few centimetres in diameter, produced by 60 pion beams which meet isocentrically at the centre of the applicator. In February 1982 curative pion irradiation of deep-seated tumours in Phase I/II studies was begun. Up to October 1984, 46 patients with pelvic diseases were irradiated by curative technique, exclusively with pions and a single course Thirty-two of these patients (70%) were treated for bladder cancer, eight (17%) for cervical cancer and six (13%) for such other tumours as rectal cancer (two patients), corpus cancer (one patient), or soft-tissue sarcoma (two patients) Treatment time was 4–6 weeks, four fractions weekly, single dose 165–200 cGy (90% isodose), total dose 300–3600 cGy (minimum tumour dose).

Ten out of 39 patients (26%) with a follow-up time of more than 6 months developed Grade 3/4 (EORTC score) late rectal complications: six of 27 patients with bladder cancer, one of three with rectal cancer, one of two sarcoma patients and two of eight patients with cervical cancer. The relationships between these complications and the dose-volume histograms, the single and total dose and, particularly, the surgical intervention after pion treatment are presented and discussed.

THE RELATIONSHIP OF THE BLADDER AND THE CERVIX IN PATIENTS UNDERGOING INTRACAVITARY THERAPY

H. R. Lukka, C. J. Moore and R. D Hunter

Christie Hospital, Manchester

Clinical studies have shown a poor correlation between bladder damage and bladder dose in patients treated with radiation therapy for uterine tumours. This study was undertaken to investigate prospectively the relationship between the cervical os and bladder in patients undergoing intracavitary treatment.

The CT scans of 59 patients undergoing intracavitary treatment were analysed. The upper limit of the undistended bladder relative to the os extended from 5.5 cm above the cervix to 4.0 cm below. The distance from the central tube to the posterior bladder wall ranged from 1.5 cm to 4.2 cm. This was positively associated with size of ovoid ($p = 0.022$), though with considerable individual variation. A separate analysis failed to show a consistent correlation with age or stage of disease. Thirty-nine of the 59 patients (65.5%) had asymmetrical bladders. Of these, half had "slight" asymmetry and the others had "marked" asymmetry. The thickness of the vesico-vaginal septum varied from 0.5 cm to 2.9 cm but was difficult to assess in some patients.

The investigations show a marked variation in bladder position relative to the cervix. In patients treated with medium ovoids and those with Ib and IIb disease the distance to the bladder base is greater than the others, though with marked individual variation. The position of the bladder cannot be accurately predicted by clinical criteria and requires to be defined by a radiological technique in the individual patient.

CONTACT THERAPY OF TUMOUR RECURRENCES IN THE REGIONS OF THE PHARYNX AND ORAL CAVITY BY MEANS OF A REMOTE-CONTROLLED AFTERLOADING TECHNIQUE

M Bauer, R. Schulz-Wendtland, H Kuttig and P Fritz

Radiotherapy Centre of the University of Heidelberg

Twelve patients with recurrent carcinomas of squamous cell epithelium were treated by contact-irradiation using a remote-controlled afterloading technique. Special applicator dentures, adapted to tumour situation and anatomy, allow a stable and reproducible positioning of the sources at the tumour. The irradiation scheme is based upon the transformation of the source co-ordinates from the stereoradiographic localisation system into the co-ordinate system of the computed tomogram. At least three fixed metal points inserted in the applicator denture and visualised by stereoradiography as well as by CT serve as mutual reference points for both co-ordinate systems. The source positioning in the tumour region is optimised by CT irradiation planning. One case is presented in order to describe the principles of the method. Preliminary results are discussed.

HOW SHOULD WE MANAGE GLOMUS JUGULARE TUMOURS IN 1986?

P J. D K. Dawes, C C. Gaffney and G Lambert

Regional Radiotherapy Centre and Regional Medical Physics Department, Newcastle General Hospital

Between January 1956 and December 1984 53 patients suffering from glomus jugulare tumours were seen in Newcastle upon Tyne. Three of these patients with tumours localised to the tympanum were treated by excisional surgery alone. The other 50 patients received some radiotherapy. Three had treatment for bilateral tumours. The actuarial survival of the radiotherapeutically treated patients was 93% at 20 years. The disease-free survival was 75% at 20 years. A dose—response curve was constructed and it suggests that a dose of 5000 cGy in 25 daily fractions will satisfactorily control the disease. Because the disease has such a potentially good prognosis, the emphasis in treatment planning must depend on low morbidity investigations (*e.g.* digital subtraction angiography) and accuracy. Accuracy in delivering the radiation dose to the tumour and avoiding sensitive normal structures can be achieved by the manufacture of well fitting treatment shells. Angled shadow blocks made individually from a low melting point alloy have been introduced recently to improve the distributions. An assessment of their effect is included.

INTRATHECAL TARGETED THERAPY FOR NEOPLASTIC MENINGITIS WITH RADIOLABELLED MONOCLONAL ANTIBODIES. A REPORT OF THREE CASES

H B. Coakham, R. B. Richardson, A. G Davies, S. P. Bourne, *D. H. Jones and *J. T. Kemshead

*Department of Neurosurgery and Medical Physics, Frenchay Hospital, Bristol and *Imperial Cancer Research Fund Laboratory, Institute of Child Health, London*

We have studied the intrathecal administration of radiolabelled monoclonal antibodies (MCA) to three cases of neoplastic meningitis in the cerebrospinal fluid (CSF) space. The first patient, with a pineocytoma, was given a diagnostic amount of ^{131}I UJ181.4 (antineuroblast MCA) with a ^{125}I control MCA which produced specificity ratios of over 20 : 1 (external counting) and 10 : 1 (CSF cell pellet). A therapeutic dose of 890 MBq (24 mCi) of ^{131}I UJ181.4 resulted in marked clinical improvement and a continuing remission (1 year). The second patient, with a B-cell lymphoma, was initially given tracer doses of ^{131}I F8-111 (anti B-cell) with a radioiodinated control MCA. This was followed by a therapeutic dose of 1560 MBq (42 mCi) of ^{131}I F8-111 alone. The third patient, a 3-year-old child with a teratoma, was given a therapeutic dose of 430 MBq (12 mCi) of ^{131}I UJ181.4 divided intrathecally and intraventrically. The biokinetics was determined by scintigraphy (blood, CSF and urine samples). The distribution and clearance of the diagnostic doses were found to be representative of the therapy doses 1–2 weeks later. The maximum activity in the blood for Cases 1 and 3 was at 45 and 54 h after injection respectively, at less than 30% of the injected dose. Case 2 experienced rapid excretion of MCA from the CSF space, with peak activity in the blood at about 20 h; no activity was seen in the head due to a basal block in the CSF space as seen by scintigraphy. An initial diagnostic study has been found to be essential to determine a patient's CSF dynamics, antibody specificity, and the radiation dose delivered, prior to antibody targeted therapy.

COMPLICATIONS AND 5-YEAR RESULTS OF TREATMENT OF CARCINOMA OF THE CERVIX USING THE CATHETRON IN RURAL INDIA

V. Balasundaram, K. Koteshwer Rao and J. G. R. Solomon

Department of Radiotherapy & Oncology, Kasturba Hospital, Manipal-576 119, Karnataka, India

The Cathetron, an automatic remote controlled afterloading device for treatment of carcinoma of the cervix, was first described by O'Connell et al in 1965. This machine has been used in Manipal for treatment of carcinoma of the cervix for more than 6 years, using the treatment regimen for early and late cases as described by Joslin in 1971. Most of the complications using high dose-rate afterloading are supposed to appear within 3 years. We presented our early experience of treating 186 cases of carcinoma of the cervix and uterus with the Cathetron at the Encuentro of the working party meeting held in Mexico, August 1982. The 4-year survival rates and complications were reported at the Encuentro following the working party meeting held at Bangkok and Pattaya, January 1985, in which we analysed our results by the life table or actuarial survival method, and an overall survival of 77% and 63% disease-free survival were found. The figures for UICC Stage IB (49 cases) were 93% and 89% respectively. The following major complications were encountered up to 4 years: radiation proctitis, five cases; stricture rectum, two cases; intestinal obstruction with gangrenous loop of bowel, one case; vesico vaginal fistulae, two cases; obstructive uropathy requiring ureterostomy, one case.

The 5-year results are presented at this conference.

THE STUDY OF ZINC IN ONCOLOGY

L. Grant

Glasgow Institute of Radiotherapy and Oncology

At the 3rd Annual Congress of ESTRO a poster was used to illustrate the effects of zinc supplements on the healing of radionecrosis, and the relationship of zinc to the pituitary—adrenal axis and stress mechanisms. Acceleration of tumour growth in C3H mice implanted with mammary adenocarcinoma has also been found in zinc supplemented animals. Considerable variation in urinary zinc outputs and plasma levels in patients undergoing radiotherapy have been found which reflect catabolic/anabolic sequences.

This paper discusses the behaviour of untreated metastases from anaplastic tumours after radiotherapy to the primary. It is concluded that the rate of cell division in such metastases mirrors the catabolic or anabolic status of the patient to the extent of making the timing of chemotherapy significant.

VAGINAL PACKING AND ITS INFLUENCE ON DOSE-RATE TO THE CRITICAL STRUCTURES DURING PELVIC BRACHYTHERAPY. A CASE REPORT

E. Dvořák and S. Song

Department of Radiation Medicine, Georgetown University, Georgetown Radiation Medicine Associates, Clinton, Maryland, USA

The indications for vaginal packing during pelvic brachytherapy are discussed. A case history is presented where the packing had to be removed in a semi-emergency situation, and was accomplished without disturbing the applicators.

A 64-year-old multipara with endometrial carcinoma, Stage IIB, was referred for pre-operative radiotherapy. She received whole-pelvis irradiation followed by the insertion of a Fletcher-Suit afterloading applicator system. Several hours following the insertion, she developed vaginal and hypogastric burning sensation not responding to diphenhydramine hydrochloride. A vaginal tear or hypersensitivity to packing gauze impregnated with sulfonamide was suspected, even though the allergy history was negative. Upon the removal of the packing, the vaginal mucosa showed focal hyperaemia with a few erosions resembling aphthae. To prevent the applicators from slipping, a short saline-soaked gauze was inserted into the vagina and the major labia was sutured. Detailed dosimetric data are presented to demonstrate that packing can be removed pending the resimulation with new dosimetric calculations without prohibitively increasing the dose to the critical structures.

Royal College of Radiologists' George Simon Lecture (sponsored by Picker International)

RALEIGH'S REVENGE

N. M. Bleehen

Department of Clinical Oncology, Addenbrooke's Hospital, Cambridge

Four centuries after the introduction of tobacco from the New to the Old World, it has become one of the major killers in modern society. Scientific and social awareness of the problem has yet to make a major impact on the prevention of the majority of tobacco-related diseases, which kill around one million people a year.

The treatment of lung cancer is still relatively unsuccessful. Surgery is only appropriate for a small proportion and curative for even less. Non-surgical treatments with radiotherapy and chemotherapy have only made an impact in small cell lung cancer. Improved diagnostic and therapeutic techniques are required and these requirements are discussed.

Proceedings of The British Institute of Radiology

Biological Basis of Radiological Protection and its Application to Risk Assessment: One Day Seminar

Chairman: Professor R. J. Berry

Cancer induction and non-stochastic effects, by Professor A. C Upton
Hereditary effect of radiation—some evidence from animal experiments, by Dr M. F. Lyon
Embryo and fetus, by Dr R. H. Mole

Chairman: Dr F. D. Sowby

ICRP recommendations, by Dr M. C. Thorne
Practical implementation of ICRP recommendations, by Mr P. F. Beaver
Radiation risks in perspective, by Sir Edward E. Pochin

CANCER INDUCTION AND NON-STOCHASTIC EFFECTS

A. C. Upton

Institute of Environmental Medicine, New York University Medical Center, USA

The mechanisms of carcinogenesis are not known in detail, but there is strong evidence that cancer usually arises from a single transformed cell. Hence, although the process of carcinogenesis appears to require a multiplicity of changes in the affected cancer-forming cell (such as may be associated with successive stages of tumour initiation, tumour promotion, and tumour progression), only one such change induced by radiation in an appropriate cell may be conceived to increase the probability of neoplasia in a suitably susceptible individual. For this reason, carcinogenic effects of radiation, like mutagenic effects of radiation, are considered for purposes of radiological protection to have no threshold and to behave as stochastic phenomena In contrast, certain other effects of radiation, such as cataract of the lens, infertility, and depression of the bone marrow, require the killing of many cells in the affected organs. Thus they vary in severity with the extent of cell loss and have thresholds of detectability which depend on the sensitivity with which the consequences of cell loss can be measured.

HEREDITARY EFFECTS OF RADIATION: SOME EVIDENCE FROM ANIMAL EXPERIMENTS

M. F Lyon

MRC Radiobiology Unit, Chilton, Oxfordshire

Data on hereditary effects of radiation in man remain very limited, and hence estimation of genetic hazards is based largely on results from animals

In males extensive work on gene mutations and chromosome aberrations has shown that not only reduction of dose-rate but also fractionation of the dose can reduce the mutational yield, and such effects may be due to changes in the cell population structure with prolonged or repeated treatment. In female mice the dose–response relationship for gene mutation is curved, probably due to the effects of DNA repair Mouse primary oocytes, which receive the major part of the lifetime dose, are very insensitive to mutation by radiation, but it is not yet known whether all species are equally insensitive.

A major part of the incidence of genetic disease in man is due to conditions of complex or irregular inheritance, such as congenital malformations. There has been doubt whether the incidence of such diseases would be altered by a change in mutation rate. It is now known that the frequency of congenital malformations among the offspring is increased by irradiation of either male or female mice before conception and the effect can be transmitted to the second generation However, the increases are relatively small

Similarly, until recently there has been doubt whether chromosomal non-disjunction (which in man is a cause of Down's syndrome) was increased by irradiation. Dose–response curves for the induction of non-disjunction in mature or growing oocytes of mice have now been obtained. However, the work involved relatively high doses and sensitive stages. The effects of low dose-rates, and in primary oocytes, remain to be investigated

EMBRYO AND FETUS

R. H Mole

Oxford

The past few years have shown major changes in attitudes to problems of irradiation of the baby developing *in utero*. Emphasis has switched from the first few weeks after conception and the possibility of unwitting exposure of conceptus or embryo, to a much later stage of development, the third to fifth lunar months after the last menstrual period At this early fetal stage the fore-brain is the most radiosensitive organ The observations and concepts leading to this change are discussed.

ICRP RECOMMENDATIONS

M. C. Thorne

International Commission on Radiological Protection, Sutton, Surrey

The current recommendations of the ICRP, published in 1977, identify two types of effect against which protection is required "Stochastic" effects are those for which the probability of an effect occurring, rather than its severity, is regarded as a function of dose without threshold, whereas "non-stochastic" effects are those for which the severity varies with the dose and for which a threshold may occur The system of dose limitation recommended by the ICRP is based on the prevention of non-stochastic effects and limitation of the probability of stochastic effects to levels deemed to be acceptable

The prevention of non-stochastic effects is achieved by setting dose-equivalent limits at values such that no threshold dose would be reached, even following exposure for the whole of a lifetime or for the total period of a working life. The limitation of stochastic effects is achieved by keeping all justifiable exposures as low as is reasonably achievable, economic and social factors being taken into account, subject to the constraint that reductions in collective exposure do not cause unacceptably large individual exposures.

The formulation of a quantitative system of dose limitation based on these principles requires that judgments be made on several factors including.

(a) relationships between radiation dose and the induction of deleterious effects for a variety of end-points and radiation types,
(b) acceptable levels of risk for radiation workers and members of the public;
(c) methods of assessing whether the cost of introducing protective measures is justified by the reduction in radiation detriment which they will provide

In the case of patients deliberately exposed to ionising radiations, the objectives of radiation protection differ somewhat from those applying to workers and members of the public For patients, risks and benefits relate to the same person, and upper limits on acceptable risks may differ grossly from those appropriate to normal individuals For these reasons, and because of its historical relationship with the International Congress of Radiology, the ICRP has given special consideration to radiation protection in medicine and has published reports on protection of the patient in diagnostic radiology and in radiation therapy

PRACTICAL IMPLEMENTATION OF ICRP RECOMMENDATIONS

P. F. Beaver

Health and Safety Executive, London

The presentation describes how ICRP recommendations are transmitted to the Government of the UK and the scrutiny which they undergo in that process The essential features of any legislation, namely clarity and enforceability, are identified, as is the part played by consultation with persons affected The practical outcome in terms of regulations and codes of practice is described in general terms and specific examples are taken from the regulations and codes showing how the principal aspects of ICRP recommendations bearing on radiation risks have been incorporated The presentation argues that the value of ICRP recommendations to the drafter of legislation is their general acceptability, giving a firm basis for requirements, against which too frequent and too positive detailed recommendations provide an unfortunate offset

RADIATION RISKS IN PERSPECTIVE

E. E. Pochin

National Radiological Protection Board, Chilton, Oxfordshire

In using radiobiological or epidemiological data for radiation risk assessments, it is important to express a realistic perspective on the sizes and kinds of risk involved, in relation to other risks to which people are normally exposed

For ionising radiation, as for other agents that may have carcinogenic or mutagenic effects which are induced without threshold and expressed after long latency, estimates of risk must be predictive. It is, therefore, particularly necessary to review the uncertainties involved in such risk assessments Similar uncertainties apply to many of the occupational or public risks with which radiation risks need to be compared. Moreover, the differences in kind of these various risks, and the different circumstances under which they are incurred, call for a broader review than only of the numerical probabilities of stated harmful effects.

Uncertainties affecting radiation risk estimates for individual organs include various questions: which organs continue to develop malignancies long after exposure, as in the thyroid and lung, or fail to do so, as for leukaemia and bone sarcoma; how should total cancer induction be derived from data on individual organs, what is the likely form of the dose–effect relationship for high and low LET radiations at low dose; and how should the induction rate for curable cancers of different organs be estimated?

Risks of causing inheritable abnormalities depend substantially upon inferences from effects in rodents, with some uncertainties in man about the detriment from effects of multifactorial determination or of recessive mutations, and on differences in sensitivity of male and female germ cells. Risks of inducing developmental abnormalities depend critically upon whether even a small threshold is likely to apply in the causation of mental retardation or of lowering of intelligence quotients

Such uncertainties, and problems in achieving the necessary comparisons with other risks, are discussed

Note full papers from this seminar will be published together in a forthcoming issue of the Journal

Proceedings of The British Institute of Radiology

Radiation Protection

Chairman: Mr D. Gifford

Measurements of the relative biological effectiveness of 24 keV neutrons, and their implications for radiation protection, by Dr P. D. Holt, Dr G. R. Morgan, Mr C. J. Roberts and Mr J. A. B. Gibson

Radiation doses and risks to neonates in a special care baby unit, by Dr K. Faulkner and Miss J. L. Barry

The effect on staff exposures during interventional radiology, following the introduction of an L/U-arm digital fluorographic system, by Miss J. Clark and Dr B. Heaton

The dose-rate levels around patients containing radionuclides for diagnostic purposes, by Dr K. J. Ugboma, Dr M. F. Cottrall and Dr A. J. W. Hilson

A national survey of doses to patients during 10 common types of X-ray procedure in England, by Dr P. C. Shrimpton and Mr B. F. Wall

Towards the development of guidelines for radiographic practice to prevent radiogenic cancers in diagnostic radiology, by Dr I. P. Matthews and K. Rogers

MEASUREMENTS OF THE RELATIVE BIOLOGICAL EFFECTIVENESS OF 24 KEV NEUTRONS, AND THEIR IMPLICATIONS FOR RADIATION PROTECTION

P. D. Holt, G. R. Morgan, C. J. Roberts and J. A. B. Gibson

Environmental & Medical Sciences Division, Harwell Laboratory, Didcot, Oxfordshire

Measurements have been made of the relative biological effectiveness (RBE) of a high-intensity filtered beam, consisting mainly of 24 keV neutrons from the PLUTO reactor, for the production of cell killing and chromosome aberrations in stationary-phase Chinese hamster (V79) cells. The RBE for cell killing, relative to acute X rays, was 2.2±0.5 at a 37% survival level, and 2.7±0.6 at low doses. Similar values were obtained for the production of dicentrics. The dose mean linear energy transfer (LET) of the neutron spectrum was 62 keV μm^{-1}. Our RBE values are lower than those measured by Thacker et al (1979) for V79 cells using track segment irradiations at similar values of LET, and the values are also lower than those measured in V79 cells by Hall et al (1975) for neutrons of higher energy but similar mean values of LET. The implications of these results for radiation protection are considered.

REFERENCES

HALL, E. J., NOVAK, J. K., KELLERER, A. M., ROSSI, H. H., MARINO, S. & GOODMAN, L. J., 1975. RBE as a function of neutron energy. *Radiation Research, 64*, 245–255.

THACKER, J., STRETCH, A. & STEPHENS, M. A., 1979. Mutation and inactivation of cultured mammalian cells exposed to beams of accelerated heavy ions. II. Chinese hamster V79 cells. *International Journal of Radiation Biology, 36*, 137–148.

RADIATION DOSES AND RISKS TO NEONATES IN A SPECIAL CARE BABY UNIT

K. Faulkner and *J. L. Barry

*Physics Department, Christie Hospital and Holt Radium Institute, Manchester and *X-ray Department, Hope Hospital, Salford*

Neonates in a special care baby unit often require radiography to follow the progress of their treatment. This may mean that neonates have a large number of radiographs during their stay in hospital. The initial aim of this study was to calculate the radiation dose to neonates from a knowledge of the technique factors, tube output and backscatter factors. Doses to a number of organs were determined from normalised organ-dose data. Somatic and genetic risks were estimated from the radiation doses to these organs. After this initial study, it was decided to attempt to reduce the radiation dose and, therefore, the risks, by altering the technique factors. In addition, a lead rubber adjustable collimator was introduced which was adapted from an earlier design (Appleton & Carr, 1984). Radiation doses and risks were then calculated and compared with the results of the initial study. Preliminary results indicate that both the radiation dose and risks have been reduced. In particular, the total body dose has been reduced from 1.6 mGy to 0.4 mGy.

REFERENCE

APPLETON, M. B. & CARR, R. S., 1984. Radiation protection in a neonatal intensive unit: a practical approach. *Radiography, 50*, 137–141.

THE EFFECT ON STAFF EXPOSURES DURING INTERVENTIONAL RADIOLOGY, FOLLOWING THE INTRODUCTION OF AN L/U-ARM DIGITAL FLUOROGRAPHIC SYSTEM

J. Clark and B. Heaton

Department of Bio-Medical Physics and Bio-engineering, University of Aberdeen

The radiation doses to the fingers of radiologists performing interventional radiology at Aberdeen Royal Infirmary are discussed. First results from finger monitoring indicate that certain radiologists who regularly perform these procedures (on units with undercouch tubes and units with overcouch tubes) approach the reference level recommended by the ICRP for occupational exposure to radiation. A digital fluorographic system has recently been installed in the hospital, and a comparison is made of the finger doses received when interventional radiology is performed on this unit with those resulting from conventional screening units.

THE DOSE-RATE LEVELS AROUND PATIENTS CONTAINING RADIONUCLIDES FOR DIAGNOSTIC PURPOSES

K. J. Ugboma, M. F. Cottrall and A. J. W. Hilson

Royal Free Hospital School of Medicine, London

Measurements have been made of the dose-rates at various positions around patients to whom pharmaceuticals have been administered for diagnostic purposes. Time and motion studies have also been made of various procedures to enable predictions to be made of the dose which is likely to be received by staff in a nuclear medicine department. The results are discussed in comparison with theoretical predictions, and simple rules for use in radiation protection calculations have been developed. Implementation of the new regulations requires consideration of the status of clinical and laboratory areas, and the exposure of individuals who enter them. The work described provides evidence for the justification of the use of time-average dose-rates and enables recommendations to be made in compliance with the ALARA principle.

A NATIONAL SURVEY OF DOSES TO PATIENTS DURING 10 COMMON TYPES OF X-RAY PROCEDURE IN ENGLAND

P. C. Shrimpton and B. F. Wall

National Radiological Protection Board, Chilton, Didcot

Diagnostic radiology is the predominant man-made source of ionising radiation for the UK population. A survey has recently been completed to establish current levels of exposure for patients undergoing 10 important types of routine X-ray examinations. Comprehensive dose information has been determined for nearly 3200 adult patients attending 20 randomly selected English hospitals. Measurements were made with a transmission ionisation chamber to record the total exposure-area product for each examination and with thermoluminescent dosemeters attached to the patient's skin. This approach has enabled the derivation of both the mean energy imparted to the patient and the doses to all the major radiosensitive organs using the results from an extensive series of Monte Carlo computer calculations employing a mathematical phantom.

The design and techniques of the survey are briefly described and results are discussed for various measured and calculated dose quantities. Histograms are presented illustrating the wide distributions often observed in the doses for each type of examination. It is hoped that the basic data from this survey will represent a useful baseline for any future dose measurements on patients. Furthermore, the present study will enable the assessment of the radiation risks from the selected radiological procedures.

TOWARDS THE DEVELOPMENT OF GUIDELINES FOR RADIOGRAPHIC PRACTICE TO PREVENT RADIOGENIC CANCERS IN DIAGNOSTIC RADIOLOGY

I. P. Matthews and K. Rogers

Department of Epidemiology & Community Medicine, University of Wales College of Medicine, Cardiff

The exposure of very large numbers of people to low doses of diagnostic radiation may produce of the order of 300 extra cancers in the population exposed, according to current estimates. A survey of patient exposures in diagnostic X-ray departments throughout Wales began in October 1983. The study is being conducted under the auspices of the Royal College of Radiologists (RCR) with funding from the Medical Research Council. A large variation in patient exposure has been found to exist between departments for a given examination. Practitioner choices with regard to projection, film–screen combination, number of exposures per procedure, size of film, kilovoltage and filtration etc all contribute to the wide range of exposures observed. The relative significance of the factors determining this variation was computed and the distribution of exposure was obtained for each of the 11 most frequently performed procedures. Based on this information, it is estimated that approximately 80% of the substantial number of extra cancers arising from these examinations could be prevented by implementation of suitable guidelines aimed at reducing interdepartmental variations in patient exposure. The development of guidelines will follow the sequence adopted by the RCR for pre-operative chest radiography and skull radiography.

Uroradiology Update

Chairman: Dr J. B. Penry

Four dimensions in uroradiology, by Professor T. Sherwood
The present state of ultrasound in the urinary tract, by Dr J. Haworth
Radionuclide imaging of the urinary tract, by Professor E Rhys Davies
Percutaneous renal angioplasty in the management of renovascular hypertension and in the preservation of renal function, by Professor R. G. Grainger and Dr D. C. Cumberland, and A. Proctor

FOUR DIMENSIONS IN URORADIOLOGY

T. Sherwood

Addenbrooke's Hospital, Cambridge

Radiological investigation of the urinary tract rested on structural studies alone for the first quarter of this century, plain radiograph and retrograde pyelogram. The intravenous pyelogram then dominated everything until some 20 years ago. By turning into the intravenous urogram (IVU), the technique added grand new areas of interest for study. Firstly, the structure of renal parenchyma could be discerned in the nephrogram. Secondly the IVU was full of functional information in regard to renal excretion and urine transport. Teasing all this apart, and understanding the potential and the limitations of these various components, had to wait almost another half century. Studies of contrast medium excretion and of acute versus chronic obstruction in the 1960s helped to clarify functional events seen on the IVU. The structural limitations, already obvious on angiography, became clearer in the 1970s with the arrival of CT.

The most important developments for urinary tract diagnosis have advanced in two directions separating structural and functional studies: ultrasound and radionuclide techniques. Because these are effective and of reasonable cost, they have between them ousted the IVU. There are good and bad reasons for clinging to the IVU as an occasional toehold. Departments certainly have to rethink their allocation of resources on urinary tract studies, including interventional manoeuvres.

THE PRESENT STATE OF ULTRASOUND OF THE URINARY TRACT

J. M. Haworth

Southmead Hospital, Bristol

Ultrasound is increasingly in demand as an investigation forming part of the basic diagnostic pathway of urinary-tract abnormalities Its major influence in the upper urinary tract remains in the differential diagnosis between solid and cystic lesions of the kidney found at excretion urography. The distinguishing features between a simple cyst, solid tumour and necrotic tumour and the identification of malignancy within a cyst are well known to all I therefore concentrate on some aspects of the use of ultrasound in the lower urinary tract, and in particular ultrasound examinations of the scrotum

Ultrasound of the scrotum has been performed in well over 110 men, with a variety of scrotal pathologies Although many are easily amenable to diagnosis by clinical examination, this is at times frustrated by local tenderness, tense intrascrotal fluid collections or gross disorganisation of the anatomical landmarks by the diseased process. It is in these cases that the value of ultrasonography of the scrotum has enabled the distinction between tense hydrocoeles and epididymal cysts, and, most importantly, the identification of the underlying normal testicle. The differentiation between an inflammatory process and tumour is also feasible, by paying particular reference to the longitudinal diameter of the epididymis Differentiation between the various tumour types has not proved as reliable. Several cases of intratesticular abscess have also been correctly diagnosed pre-operatively The operative management of cases of trauma have also been influenced by demonstrating that the testicle itself is intact, underlying the accompanying haematoma In cases with acute inflammatory epididymo-orchitis, follow-up scans have indentified a group which show the changes of post-inflammatory infarction of the testicle. Work is proceeding to try and see if there are indentifiable features on the initial scan, which can predict the outcome of infarction.

Ultrasound remains a cheap, non-invasive method of investigation for a wide range of intrascrotal pathologies

RADIONUCLIDE IMAGING OF THE URINARY TRACT

E. Rhys Davies

University of Bristol

The subject is briefly reviewed

PERCUTANEOUS RENAL ANGIOPLASTY IN THE MANAGEMENT OF RENOVASCULAR HYPERTENSION AND IN THE PRESERVATION OF RENAL FUNCTION

R. G. Grainger, *D. C. Cumberland and *A. Proctor

*Royal Hallamshire Hospital and *Northern General Hospital, Sheffield*

All 35 patients subjected to percutaneous transluminal renal angioplasty for renal artery stenosis in Sheffield have been followed for up to 45 months Of 18 patients with atheromatous renal artery stenosis, 17 are considerably improved with reduced hypertension and a reduction of antihypertensive drugs. Seven are now normotensive and not receiving any drugs Six patients had fibromuscular hyperplasia of one or more renal arteries, all six are improved, with reduced hypertension. One patient is normotensive without drugs Five patients had severe arterial stenosis of a transplant kidney with severe hypertension All five were improved by angioplasty and the transplant was saved in several patients. Six patients had angioplasty primarily for renal tissue salvage as they had severe arterial stenosis to a solitary functioning kidney In all six cases renal function was improved by the angioplasty and in four the hypertension was reduced. There were no significant operative complications.

Our experience in Sheffield is that percutaneous renal angioplasty is a very satisfactory procedure with low morbidity, very encouraging improvement in hypertension and considerable potential for salvage of functional renal tissue.

Hepatobiliary System and Pancreas Update

Chairman: Dr J. P. Virjee

Review—liver and pancreas, by Dr W. R. Lees

Quantitative tissue characterisation in pancreatic disease using MRI, by Dr J. P. R. Jenkins, Professor I. Isherwood and Dr J. Braganza

Revised criteria for detection of hepatic steatosis and fibrosis, by Dr A. E. A. Joseph, Dr E. J. Adam, Dr K C. Dewbury, Dr J. McKenzie and R. Hangartner

Percutaneous pancreatography—a description of the technique and a review of 75 cases, by Dr C W. Heron and Dr W R. Lees

REVIEW: LIVER AND PANCREAS

W. R. Lees

Middlesex Hospital, London

This review assesses the current status of imaging, detection and diagnosis of focal and diffuse liver disease and the most appropriate biopsy techniques are outlined for the most common clinical situations diffuse liver disease, diffuse liver disease with contra-indication to conventional biopsy, metastases, vascular liver tumours, hydatid disease, and biopsy in hepatitis and AIDS Specific diagnostic topics covered are fatty infiltration, chronic liver disease, detection of metastases and the radiological diagnosis of benign and malignant liver tumours

In the pancreas the emphasis is on the underlying pathology of pancreatic disease and how this is reflected in the morphology recognised by imaging techniques. The radiological natural history and evolution of acute pancreatitis, chronic pancreatitis, and pancreatic cancer are displayed and the role of radiology at the clinical decision points is defined.

QUANTITATIVE TISSUE CHARACTERISATION IN PANCREATIC DISEASE USING MAGNETIC RESONANCE IMAGING

J. P. R. Jenkins, I. Isherwood and *J. Braganza

*Departments of Diagnostic Radiology and *Gastroenterology, University of Manchester*

The aim of this study was to assess the role of measured relaxation times in the normal and diseased pancreas. Forty patients (age range 20–84 years) with clinical evidence of pancreatic disease were studied with MRI and dynamic contrast-enhanced CT. In eight normals, including five volunteers (age range 27–74 years) MRI alone was performed. A Picker International superconducting magnet system operating at 0.26 T was used for MRI. The MRI data included calculation of the T_1 and T_2 relaxation times and proton density using a previously described multipoint iterative method (Hickey et al, 1986), which has been used successfully in other clinical studies (Jenkins et al, 1985). An additional 8-image multisection inversion-recovery sequence was performed in the sagittal and/or coronal plane for morphological display. Of the 40 patients studied, 28 had adequate MRI data on the pancreas.

MEAN PANCREATIC T_1 AND T_2 VALUES WITH STANDARD ERRORS FOR BOTH PATIENT AND CONTROL GROUPS

	Control (n = 8)	Pancreatic tumour (n = 5)	Chronic pancreatitis		Acute pancreatitis (n = 2)
			Calcification (n = 8)	No calcification (n = 9)	
T_1	*545 ± 38	676 ± 77	*812 ± 36	*522 ± 59	545 ± 303
T_2	58 ± 2	65 ± 7	65 ± 4	55 ± 5	70 ± 2

*highly significant difference $P < 0.001$

There is a highly significant difference ($P < 0.001$) in the measured T_1 values between the control group and those patients with chronic pancreatitis who exhibit calcification on CT. Similarly a highly significant difference ($P < 0.001$) in the calculated T_1 values of the chronic pancreatitis group was found between those patients who exhibit calcification on CT and those who do not. Although calcium itself gives no MR signal, its presence has a significant effect on pancreatic relaxation times. These results indicate that calculated relaxation times can differentiate normal from some pathological pancreatic tissue.

REFERENCES

HICKEY, D. S., CHECKLEY, D. R., ASPDEN, R. M., NAUGHTON, A., JENKINS, J. P. R. & ISHERWOOD, I., 1986. A method for the clinical measurement of relaxation times in magnetic resonance imaging. *British Journal of Radiology*, 59 (in press).

JENKINS, J. P. R., HICKEY, D. S., ZHU, X. P., MACHIN, M. & ISHERWOOD, I., 1985. Magnetic resonance imaging of the intervertebral disc: a quantitative study. *British Journal of Radiology*, 58, 705–709.

REVISED CRITERIA FOR THE DETECTION OF HEPATIC STEATOSIS AND FIBROSIS

*A. E. A. Joseph, E. J. Adam, *K. C. Dewbury, †J. McKenzie and †R. Hangartner

*Department of Radiology, Nuclear Medicine and Ultrasound, and †Department of Pathology, St George's Hospital, London and *Department of Radiology, Southampton General Hospital*

Attenuation of ultrasound has in the past been considered a characteristic feature of cirrhosis and therefore useful in distinguishing it from steatosis alone. Other authors have stated that beam attenuation is a variable feature with steatosis. These conclusions have been drawn using 3.5 MHz and 2.25 MHz frequencies. Our studies, using 5 MHz frequency, indicate that beam attenuation is a characteristic feature of steatosis. In mild cases, when 3.5 MHz frequency was used, this effect disappeared and the characteristic echo texture obtained with 5 MHz was lost. Moderate to severe steatosis, however, does show some degree of beam attenuation with 3.5 MHz frequency.

We also found that fibrosis alone, in the absence of steatosis is not associated with beam attenuation. Beam attenuation, when seen in cirrhosis, is probably due to accompanying fatty change.

The ultrasound findings were correlated with histological evidence obtained by liver biopsy or at post-mortem examination in 85 patients. We conclude that beam attenuation should be considered a characteristic feature of steatosis when using 5 MHz frequency, and that this should be used routinely. Good beam penetration should be considered characteristic of cirrhosis or fibrosis unaccompanied by steatosis. These revised criteria are a complete reversal of those stated in the literature hitherto.

PERCUTANEOUS PANCREATOGRAPHY. A DESCRIPTION OF THE TECHNIQUE AND A REVIEW OF 75 CASES

C. W. Heron and W. R. Lees

Department of Imaging, The Middlesex Hospital, London

Since 1982, percutaneous pancreatography under ultrasound guidance has been employed at The Middlesex Hospital to assist in the diagnosis and management of a select group of patients. We describe the technique and present our experience of the first 75 cases performed in this department.

The main purpose of the procedure is to assist in tumour localisation in fine-needle aspiration biopsy (FNAB) of the pancreas. Our results demonstrate that when a combination of radiographic localisation by percutaneous pancreatography and ultrasound guidance is used, the sensitivity of FNAB is increased. The technique is also useful in order to document accurately the appearance of the pancreatic duct prior to pancreatic surgery. It is particularly applied in cases where endoscopic retrograde pancreatography may not be possible, for example in some patients with a history of previous gastric surgery or pancreas divisum. Percutaneous pancreatography has been used in addition to evaluate pancreatic masses occurring in patients with concurrent chronic pancreatitis. In this instance pancreatography has enabled differentiation of areas of inflammation from carcinoma.

We conclude that percutaneous pancreatography is a safe and reliable technique which may be performed using standard ultrasonic equipment. It plays a valuable role in the investigation of selected patients with pancreatic disease.

Proceedings of The British Institute of Radiology

Cardiac Radiology

Chairman: Professor I. Isherwood

Heart size in AP chest radiographs, by Dr J. E. Kabala and Dr P Wilde

The anatomical and pathological basis for ECG changes during selective coronary arteriography, by Dr M. Papouchado, Dr D. W. Pitcher, Dr M A. James, Dr P. R. Walker and Dr P. Wilde

MRI in the assessment of coronary artery bypass graft patency, by Dr J. P. R. Jenkins, Dr H. G. Love, Dr C J. Foster, Professor I. Isherwood and Dr D. J Rowlands

Non-invasive monitoring of left ventricular function using pulsed Doppler ultrasound, by Dr K S. Channer, Dr W Culling, Dr P Wilde and Dr J V Jones

Dipyridamole combined with exercise in ^{201}Tl cardiac imaging, by Dr C. Hamilton-Wood, Dr P. R. Walker, Dr M. A. James and Dr P Wilde

Myocardial imaging with 17-(123-iodo)-heptadecanoic acid, by Dr P G. P. Stoddart, Dr M. Papouchado and Dr P. Wilde

Dynamic phase and amplitude analysis of gated cardiac studies, by Dr B. L Rahimi, Dr R. J Burwood, Dr S. W. Ellacott and Dr J. E. Lutkin

Cine CT—a new imaging technique for cardiac disease, by Dr M R. Rees, Dr W J. Eldredge, Dr R. M MacMillan and Dr D. L Clark

Imaging of adult and paediatric heart disease by cine CT using new oblique views, by Dr M. R. Rees, Dr R M MacMillan, Dr W. J. Eldredge, Dr A J. Feiring, J A. Rumberger, H. Naidech and Dr D. L Clark

A new method for display of anatomical and functional information obtained by magnetic resonance on a single colour image, by Dr R. H. Klipstein, Dr D. N. Firmin, Dr S. R. Underwood, Mr G. L. Nayler and Dr D. B. Longmore

HEART SIZE IN ANTERO-POSTERIOR CHEST RADIOGRAPHS

J E. Kabala and P. Wilde

Department of Radiodiagnosis, Bristol Royal Infirmary

Heart size is usually measured on a PA film, but the patient's condition may prohibit this The alternative use of an AP film is traditionally considered unsatisfactory because of variables that include focus-film distance, magnification and the AP relationship of the heart to the chest wall. The contribution of these variables was studied in order to establish a standardised approach and define its limitations. The effects of cardiac disease were assessed by measuring cardiothoracic ratio (CTR) and transverse heart diameter (TD) on technically satisfactory standardised AP chest radiographs of two groups of patients

Group A. 103 patients with no clinical, historical or other evidence of heart disease or failure; 96% (99/103) had a CTR of 55% or less (median CTR 50%) and a TD of 165 mm or less

Group B 106 patients with known cardiac failure, 92% (97/106) had a CTR greater than 55% (median 62%) and 90% (95/106) had a TD above 165 mm

It is shown that upper limits of 165 mm (TD) and 55% (CTR) allow useful discrimination of normal from abnormal heart size

THE ANATOMICAL AND PATHOLOGICAL BASIS FOR ELECTROCARDIOGRAPHIC CHANGES DURING SELECTIVE CORONARY ARTERIOGRAPHY

M Papouchado, D W. Pitcher, M. A. James, P R. Walker and *P. Wilde

*Departments of Cardiology and *Radiodiagnosis, Bristol Royal Infirmary, Bristol*

Electrocardiographic changes during selective coronary arteriography are well recognised but have not hitherto been closely correlated with coronary anatomy and pathology Two simultaneous ECG leads (I or aVL and II, III or aVF) were recorded during each of 927 selective coronary injections in 185 patients. Coronary anatomy was assessed in each case using a detailed diagrammatic reporting technique Electrocardiographic changes were of two main types a perfusion response (increase in R-wave amplitude and T-wave inversion) or an opposite reciprocal response The traces were independently analysed for the presence of these responses.

Perfusion responses correlated highly with differing anatomical distribution when left and right coronary arteries were injected In particular, ECG changes reflected the differing blood supply of the inferior left ventricular surface (119 out of 126 patients with right dominant, 16 out of 20 patients with left dominant, two out of two patients with mixed dominance) In 33 out of 37 patients with left coronary injections filling occluded right dominant vessels, a delayed perfusion response was evident inferiorly Fifteen patients with extensive myocardial infarction or dilute contrast-medium injections had no significant changes Varying degrees of stenosis did not affect distribution of responses in patent arteries

MAGNETIC RESONANCE IMAGING IN THE ASSESSMENT OF CORONARY ARTERY BYPASS GRAFT PATENCY

J. P. R. Jenkins, *H. G. Love, *C. J Foster, I Isherwood and *D. J. Rowlands

*Departments of Diagnostic Radiology and *Cardiology, University of Manchester*

The patency of coronary artery bypass grafts as assessed by MRI was compared with coronary graft arteriography and/or CT Twenty patients (age range 34–63 years) were studied pre- and post-operatively by MRI performed on a Picker International superconducting magnet system operating at 0 26 T. Electrocardiogram-gated MR images were obtained in the transverse, sagittal and coronal planes using a spin-echo, multisection sequence. Coronary graft arteriography was performed in 15 patients, CT alone in four and CT combined with arteriography in three A total of 54 grafts were studied and the results are shown in the table below.

CORONARY ARTERY BYPASS PATENCY:COMPARISON OF MRI WITH CORONARY GRAFT ARTERIOGRAPHY AND/OR CT

		Arteriography/CT	
		+	−
MRI	+	31	5
	−	3	15

Sensitivity of MRI for detection of graft patency = 91%
Specificity of MRI = 75%
Accuracy of MRI = 85%

The transverse imaging plane was found to be the most useful in assessing graft patency by MRI. The reasons for the false negative and positive results are discussed in further detail. It is concluded that MRI can detect a normally functioning coronary artery bypass graft and can be used as a non-invasive method for the assessment of coronary artery bypass graft patency in patients presenting with post-operative angina.

NON-INVASIVE MONITORING OF LEFT VENTRICULAR FUNCTION USING PULSED DOPPLER ULTRASOUND

K. S. Channer, W. Culling, *P. Wilde and J. V. Jones

*Departments of Cardiology and *Radiodiagnosis, Bristol Royal Infirmary*

Haemodynamic assessment of left ventricular function has previously relied on invasive techniques. We have compared the ratio of the passive and active phases of mitral flow with left ventricular end diastolic pressure (LVEDP) measured at cardiac catheterisation in 20 patients (14 males) of mean age 51.9 (range 36–62) years with ischaemic heart disease. None had clinical evidence of aortic or mitral valve disease and all were in sinus rhythm. Pulsed Doppler measurements of mitral flow were performed in the cardiac catheter laboratory using the apical view to position the sample volume in the mitral orifice. Doppler flow signals were recorded simultaneously with an electrocardiogram and LVEDP. Each spectrally analysed mitral valve flow trace showed two diastolic peaks. The first presented passive flow down the pressure gradient from left atrium to ventricle, and the second represented active flow due to atrial contraction. The mean of 10 consecutive recordings of the ratio of the areas of the two wave forms was calculated. The ratio was significantly correlated with LVEDP ($r = 0.78$ $P < 0.001$). Active mitral flow was lower with higher LVEDP. Mitral flow ratios of > 2 were always associated with LVEDP > 20 mm Hg. This application of pulsed Doppler echocardiography provides a non-invasive method of estimating LVEDP.

DIPYRIDAMOLE COMBINED WITH EXERCISE IN THALLIUM-201 CARDIAC IMAGING

C. Hamilton-Wood, *P. Walker, *M. James and P. Wilde

*Departments of Radiodiagnosis and *Cardiology, Bristol Royal Infirmary*

A method is described in which pharmacological coronary vasodilatation with orally administered dipyridamole is combined with dynamic exercise for a new stress test for ^{201}Tl imaging. In 38 patients with coronary artery disease the sensitivity, total number of defects, degree of redistribution and visual quality of ^{201}Tl imaging were all greater after "dipyridamole-exercise" testing than after exercise alone. In a larger group of patients, dipyridamole-exercise testing gave a sensitivity for coronary disease of 87% and a specificity of 92%. Dipyridamole also increased the sensitivity of the exercise electrocardiogram, so that every patient with significant coronary disease showed scintigraphic and/or electrocardiographic evidence of ischaemia. Among a total of 193 patients, complications requiring reversal with aminophylline have occurred in five, but no subsequent mortality or morbidity was incurred. The combined use of oral dipyridamole and exercise in this simple technique provides a reliable and safe improvement in ^{201}Tl imaging.

MYOCARDIAL IMAGING WITH 17-(123-IODO)-HEPTADECANOIC ACID

P. G. P. Stoddart, *M. Papouchado and P. Wilde

*Departments of Diagnostic Radiology and *Cardiology, Bristol Royal Infirmary*

The myocardial uptake of HDA is reduced by ischaemia and infarction. However, the metabolic clearance, measured as an exponential half-life, is prolonged in ischaemic myocardium, while it is reduced in infarcted myocardium, which is irreversibly damaged. This study aimed to see if the half-life of acutely infarcted myocardium was related to subsequent changes in the left ventricular ejection fraction (LVEF). Twenty patients had an HDA scan and a MUGA scan within 6 days of acute myocardial infarction. Eighteen patients had a visible defect on the HDA images. The mean half-life of the areas of acute infarction (15.50 ± 7.82 min) was significantly shorter than that of normal myocardium (20.77 ± 4.00 min). The MUGA scan was repeated after 6 months in 15 patients. The mean acute infarct half-life was longer in patients with an LVEF improvement of at least 5% at 6 months (16.92 ± 10.56 min) than in those with more than 5% deterioration (11.75 ± 4.03 min), although the difference is not statistically significant. It was concluded that the infarct half-life of HDA cannot be used as a prognostic indicator because of the variable response in individual patients.

DYNAMIC PHASE AND AMPLITUDE ANALYSIS OF GATED CARDIAC STUDIES

B. L. Rahimi, R. J. Burwood, S. W. Ellacott and J. E. Lutkin

Department of Medical Physics, Royal Sussex County Hospital

Previous authors have reconstructed a Fourier series representation of the time–activity curves (TACs) obtained from gated cardiac studies, and taken the phase and amplitude of the first harmonic of each TAC to estimate it with a cosine curve. This is open to the objection that at any point in time, each TAC is in constant phase and amplitude relationship to every other TAC, a state of affairs which is obviously not true in practice and which hides significant cardiac information. Moreover, there are problems in reconstructing the TAC caused by the gated data acquisition. In this paper, we prove a result on reconstructing the TAC. Fourier analysis is then used to provide a multiharmonic model of the TACs, and a definition of time-dependent phase and amplitude is extracted from the model and used to produce dynamic phase and amplitude images. This is carried out by taking the discrete Fourier transform of the TAC and then representing the dynamic phase and amplitude to be the argument and the amplitude of half the terms. (The whole series simply reconstructs the TAC.) This proved to vary with time. This process is a method for representing the TAC as:

$$f(t) = A(t) \cos [\theta(t)].$$

These parameters are used to produce dynamic phase and amplitude images. A dynamic study of the rate of change of volume of the heart is also displayed. The combination of dynamic functional studies is proposed as a tool for cardiac diagnosis. The progress to date on the clinical evaluation of the technique is also presented.

CINE COMPUTED TOMOGRAPHY: A NEW IMAGING TECHNIQUE FOR CARDIAC DISEASE

M. R. Rees, *W. J. Eldredge, R. M. MacMillan and D. L. Clark

*Killingbeck Hospital, Leeds and *Deborah Heart and Lung Center, Browns Mills, USA*

The Imatron C-100 scanner is a new development in cardiac imaging which allows image acquisition at 17 images/s at eight levels simultaneously. The scan time is 50 ms with an interscan delay of 8 ms. The scanner consists of an electron gun which produces a scanning electron beam magnetically focused onto four tungsten targets, each of which generates two X-ray beams collimated to 8 mm slices. The scanner has no moving parts. Cardiac function as well as structure can be investigated (Lipton et al, 1985). Early experience based on 200 adult and 150 paediatric patients has demonstrated a wide clinical application of the technique. In the first 42 paediatric patients useful clinical information was obtained in all but one case with close agreement with catheterisation or echo (Eldredge et al, 1985a). In 10 cases of ventricular septal defect there was accurate localisation of the defect site (Eldredge et al, 1985b). The technique has also been found to be useful in complex congenital heart disease and cases of cardiomyopathy. Various cardiac disease have in adults been diagnosed by cine CT and confirmed by conventional imaging, including calcified constrictive pericarditis, mitral valve stenosis and prolapse, left ventricular aneurysm and thrombus, atrial septal defect in which it was possible to quantify the degree of intracardiac shunting, and aorto-coronary artery bypass grafts in which graft patency in 21 patients showed 92% sensitivity compared to catheterisation (Rees et al, 1985). Regional wall motion was analysed in 15 patients with comparable results to catheterisation. Prosthetic valves in 15 patients were studied and could be imaged with little streak artefact, demonstrating their movement. We conclude that cine CT can make a considerable contribution to the investigation of adult and congenital heart disease.

REFERENCES

Eldredge, W. J., Bharati, S., Flicker, S., Clark, D. L. & Lev, M., 1985a. *World congress of paediatric cardiology presentation, New York, USA, June 2–6.*

Eldredge, W. J., Rees, M. R., Flicker, S., Clark, D. L., 1985b. Cine CT scanning of the ventricular septal defect. *Presentation at the 58th Scientific Session of the American Heart Association, Washington DC, USA, November.*

Lipton, M. J., Higgins, C. B. &Boyd, D. P., 1985. Computed tomography of the heart. Evalution of anatomy and function. *Journal of the American College of Cardiologists, 5*, 55–69.

Rees, M. R., MacMillan, R. M., Reiter, S., Rumberger, J., Feiring, A., Maranhao, V. & Clark, D. L., 1985. Sensitivity and specificity of coronary artery bypass graft assessment by cine computed tomography. *Presentation at the British Cardiac Society Meeting, London, UK, November.*

IMAGING OF ADULT AND PAEDIATRIC HEART DISEASE BY CINE COMPUTED TOMOGRAPHY USING NEW OBLIQUE VIEWS

M. R. Rees, R. M. MacMillan, *W. J. Eldredge, A. J. Feiring, J. A. Rumberger, H. Naidech and D. L. Clark

*Killingbeck Hospital, Leeds and *Deborah Heart and Lung Center, Brown Mills, USA*

High-speed cine CT (17 images/s) offers a dynamic new modality for cardiac imaging. We have developed a series of oblique views for cine CT to aid investigation of cardiac anatomy and function.

a) The short-axis view (Rees et al, 1985). This allows visualisation of all the left ventricular walls and is the method of choice for accurate estimation of global ejection fraction in adults (nine cases). This view is also useful in congenital heart disease to image the pulmonary outflow tract and aortic valve and to help in the diagnosis of complex congenital heart disease (five cases). This view complements the long-axis view. In paediatric patients it is produced by a clockwise table slew of 20–25° combined with a feet downwards table tip of 20°. In adult patients a greater tip is required and the patient's torso is elevated on a foam wedge with a final angle of 20–55°. This view is analogous to the parasternal short-axis views obtained by two-dimensional echocardiography.

b) The long-axis view. This allows visualisation of all four cardiac chambers and the aortic root and images the left ventricle in its longest dimension. This view is useful in congenital heart disease to localise ventricular (10 cases) and atrial septal defects (five cases), in adult cardiology to evaluate ejection fraction (MacMillan et al, 1985) (15 cases vs catheterisation) and regional wall motion (Rees et al, 1985) (15 cases vs catheterisation). The long axis is achieved by a counterclockwise table slew of 20° without table tilt. This view is analogous to the apical four-chamber view obtained by two-dimensional echocardiography.

c) The modified long-axis view. This allows for visualisation of the aortic valve longitudinally. It is also useful to image the right ventricle in paediatric patients. This view is achieved by using 20–25° counterclockwise slew with 5–10° feet downward table tilt.

REFERENCES

MacMillan, R. M., Rees, M. R., Maranhao, V. & Clark, D. L., 1985. Presented at the 32nd Meeting of the International College of Angiology, South Carolina, USA, November 10–14. Comparison of left ventricular ejection fraction by cine computed tomography and single plane right anterior oblique ventriculography.

Rees, M. R., Ell, S. R., Jolles, H., Rumberger, J., Feiring A. & Marcus, M., 1985. Short axis view of the left ventricle obtained by cine CT. Society of thoracic radiology abstracts. *American Journal of Roentgenology, 145*, 658.

Rees, M. R., MacMillan, R. M., Maranhao, V. & Clark, D. L., 1985. Rapid acquisition computed tomographic assessment of left ventricular regional wall'motion using a new long axis view. *Presented at the 32nd Meeting of the International College of Angiology, South Carolina, USA, November 10–14.*

A NEW METHOD FOR DISPLAY OF ANATOMICAL AND FUNCTIONAL INFORMATION OBTAINED BY MAGNETIC RESONANCE ON A SINGLE COLOUR IMAGE

R. H. Klipstein, D. N. Firmin, S. R. Underwood, G. L. Nayler and D. B. Longmore

MR Unit, National Heart and Chest Hospitals, London

Gated magnetic resonance can acquire cine images of anatomical and flow information from the heart and blood vessels in a single study taking roughly 20 min. We have developed a method whereby both anatomy and blood flow can be displayed on a single image, the anatomical information in monochrome and the functional information in a colour corresponding to blood velocity.

Conversion of the anatomical and the functional images into an image suitable for the colour display is achieved by computer processing. A combination of thresholding and conditional display of functional information, depending on the magnitude of the corresponding anatomical information, avoids excessive artefact due to noise on the functional image.

Blood flow in the forward direction is displayed in one colour and in the reverse direction in another, with a brightness proportional to the speed of flow. Cine display, related to the physiology of blood flow during the cardiac cycle, is particularly informative.

Composite colour cine images in the transverse, coronal and sagittal planes, for flow within the image plane or perpendicular to it, have been constructed. Flow in normal hearts and regurgitation through incompetent valves have been observed and quantified.

Managing Radiology

Chairman: Professor E. Rhys Davies

The development of radiological services—economic influences, by Mr J. Hutton
Costs of imaging procedures, by Dr P. M. Bretland
Failure in radiodiagnostic equipment—implications for the NHS, by Mr P. H. Smithson and Mr J. A. Garrett
Economic evaluation of clinical MRI, by Mr J. Hutton
Management patterns in British CT, by Dr S. J. Golding
The evaluation of CT scanning and the lumbar spine, by Dr P. Kind, S. Sims and P. Verow

THE DEVELOPMENT OF RADIOLOGICAL SERVICES: ECONOMIC INFLUENCES

J. Hutton

Centre for Health Economics University of York

In the radiological field, research and development have consistently produced new and improved imaging methods in the post-war period. Improved clinical performance has been the measure of success, with cost-effectiveness a secondary consideration. When budgets are tightly constrained, hard decisions must be taken on the reduction of existing services if new technology is to be acquired. One way out of this dilemma is to reduce the cost of basic services to free resources for the introduction of new techniques. In this context the WHO "Basic Radiological System" (BRS), originally conceived for developing countries, could have a role in the NHS, since it is claimed that it can perform 80% of standard radiological examinations at a capital cost of one third of that of a conventional X-ray system. At the same time moves are afoot to make conventional radiography more sophisticated through digitisation of images. Proponents of this approach also claim cost savings (in operation), as well as improved performance.

How should the NHS plan the development of radiological services, given that resources are unlikely to be available for the purchase of increasingly sophisticated equipment in all sections of the service? Options include: reduction of service levels; concentration of expensive techniques in a limited number of centres, revision of clinical practice in requesting tests, and procurement of cheaper equipment for the basic workload. In assessing these options resource considerations must play a part and this paper attempts to identify the key economic factors associated with each possible policy.

COSTS OF IMAGING PROCEDURES

P. M. Bretland

Whittington Hospital, London

The principles of commercial financial management are contrasted with current NHS methods. A costing system, using standard commercial practice (classifying costs into "variable," "semi-variable", and "fixed", corresponding roughly to materials, salaries, and building and equipment maintenance) and commercially available computer software, has been devised. The whole Whittington Hospital imaging service for the financial year 1984/85 was so costed. Imaging procedures could be put into a cost spectrum in ascending order of cost as follows: plain radiographs, ultrasound, tomography, interventional ultrasound, intravenous urography, diagnostic fluoroscopy, nuclear medicine, interventional fluoroscopic procedures, diagnostic angiography and interventional angiographic procedures. Only the more expensive nuclear medicine procedures and angiography exceeded the cost of the inpatient day. The findings are considerably at variance with the Korner Report. Hypothetical calculations have been made for equipment depreciations, bearing in mind that capital costs of equipment increase annually by figures ranging from 6% for nuclear medicine to 14% for X-ray equipment, and for the capital costs of buildings using the concept of "notional rent". A plea is made for an improved costing system within the NHS, including proper considerations of equipment depreciation.

Proceedings of The British Institute of Radiology

FAILURE IN RADIODIAGNOSTIC EQUIPMENT: IMPLICATIONS FOR THE NATIONAL HEALTH SERVICE

P. H. Smithson and J. A. Garrett

Department of Medical Physics, Bristol Radiotherapy Centre

Experience has been gained in a large teaching district of over 60 rooms where in-house servicing is operated in parallel with manufacturers' servicing over the full range of radiodiagnostic equipment. This paper presents an analysis of why equipment failed over a 2-year period.

Faults analysed include those that are largely electromechanical and also some where a significant number of call-outs were due to faults that disappeared once the engineer arrived! Processors are very prone to replenisher faults and rapid wear-out. Gamma cameras and ultrasound equipment need frequent adjustment to maintain a high image standard. These results are examined to see if planned preventative maintenance is required to ensure a high operating efficiency. Unfortunately, newer systems with a large electronic content do not show the expected reduction in down time. Figures are presented to show the spare-part requirements on the various types of equipment. These results are taken from a comprehensive equipment management computerised data base in operation in the district. The resulting implications for a buying and servicing policy are discussed.

MANAGEMENT PATTERNS IN BRITISH COMPUTED TOMOGRAPHY

S. J. Golding

University of Oxford

A survey was carried out of general purpose CT installations in the UK, to determine how these are organised and the nature and volume of their workload. The majority of CT facilities are situated within existing X-ray departments and administrative responsibility for the service is usually shared between several radiologists. Irrespective of the site of the CT facility, supervision of the clinical work is carried out by consultant radiologists who are present during the examination in the majority of installations. These facts are relevant to the staffing implications of new CT services.

More than half the CT installations carry out junior staff training. Fewer of them do formal CT-assisted radiotherapy planning or non-clinical research. A significant component of the workload in many installations is CT-guided interventional procedures, the results suggest that more than 1000 such procedures are carried out in the UK each year. There appears to be a normal distribution between cranial and body work on general purpose machines, but significant differences in patient throughput exist between different installations. This variation is not explained by differences in the nature of the workload. While the availability of CT remains limited in this country, this variation is a cause for concern.

ECONOMIC EVALUATION OF CLINICAL MAGNETIC RESONANCE IMAGING

J. Hutton

Centre for Health Economics, University of York

As MRI becomes more sophisticated and the range of clinical applications expands, the demand for the technology increases, but resources for its acquisition and use in the UK do not. The University of York Centre for Health Economics has been commissioned by the MRC to carry out a cost-effectiveness study of the clinical use of MRI, in co-operation with the MRC and DHSS-financed clinical research centres. The paper presents the preliminary results of a costing study of the UK installations, and discusses the relevance of these to operation of MRI units on a service basis in the NHS. The measurement of the effectiveness of a new diagnostic technology poses even greater problems than costing. The particular difficulties of assessing MRI is discussed, and proposed research designs to overcome these problems are described.

THE EVALUATION OF COMPUTED TOMOGRAPHIC SCANNING AND THE LUMBAR SPINE

P. Kind, S. Sims and *P. Verow

*Centre for Health Economics, University of York and *X-Ray Department, York District Hospital*

Following the installation in 1981 of a CT scanner in the York District Hospital, and a subsequent review of its usefulness in the investigation of lumbar disc disease, the number of lumbar radiculograms fell dramatically. Now, CT of the lumbar spine has become the standard procedure when investigating low back problems. The number of radiculograms has fallen steadily over the 5 years of CT scanning at York, the 1984 total being only 14% of those performed in 1980. This paper examines the impact of CT scanning on the treatment and management of patients referred mainly with low back pain and sciatica. It compares the costs of radiculograms with those of CT scanning and identifies areas of potential benefit for both the clinician and the patient.

Scientific Exhibition

Adaptation of the Blomfield applicator for use with the Selectron, by H. J. Appleby, H. Eckert and T. J. Godden

Energy response of film/screen combinations, by M. Arnold, P. Liepins and N. E. Tomlinson

The *in vitro* echographic appearances of gastric wall, by J. Beynon, D. M. A. Foy, L. N. Temple, N. J. McC.Mortensen and J. P. Virjee

Staging of rectal cancer by endoluminal ultrasound, by J. Beynon, A. Roe, D. M. A. Foy, L. N. Temple, N. J. McC.Mortensen and J. P. Virjee

Inherent filtration as a function of beam angle for diagnostic X-ray tubes, by R. Bovill and R. W. Grange

A graphical dosimetry method for "Paris" brachytherapy implants, by M. P. Casebow

Post-irradiation survival of DNA synthesis in cytochalasin-treated Chinese hamster ovary cells. A flow cytometric method, by J. B. Court, C. Burn and J. L. Moore

Determination of X-ray spectra from measurements of attenuation, by D. R. Dance

K-edge filters and mammography, by D. R. Dance, R. Davis, S. H. Evans, C. H. Jones and C. A. Parsons

Computed tomography-guided cannula insertion in pelvic hyperthermia, by G. C. W. Howard, A. K. Dixon and N. M. Bleehen

Techniques for intraoral electron treatments, by F. R. Hudson, M. Samarasekara and D. Hynd

Assessing abnormal liver biochemistry: wedge hepatic venography? liver biopsy? wedge hepatic venous pressure? by D. J. van Leeuwen, P. Scheuer, S. Sherlock and R. Dick

Tumour markers in malignant teratoma: results from a study in the South-West of England, by P. A. Light and S. E. Goodman

Real-time ocular ultrasound in the management of malignant melanoma of the choroid, by N. C. McMillan

Cine computed tomography-derived left ventricular ejection fraction using a single central slice, by R. M. MacMillan, M. R. Rees and D. L. Clark

CT scanner phantom for checking electron density and distance measurements on a treatment planning computer, by A. K. Morgan, D. H. Temperton, R. G. Putney and S. C. Klevenhagen

A high-power pulsed dye laser for dynamic phototherapy of tumours, by A. W. Preece, N. P. Luckman and D. H. Follett

Computed tomography dose and image evaluation using ionisation chambers and test objects made at the London Hospital, by R. Putney, S. Dye and D. Temperton

The influence of time of day of administration of VAC chemotherapy of myelosuppression sequential serum urate and the circadian rhythm of urate excretion, by M. H. Robinson, R. Pownall and M. S. Knapp

Thallium-201 myocardial scintigraphy after voluntary hyperventilation, by J. Teijeriro-Vidal, A. Mateo, M. J. Perez-Castejon, F. Garcia and E. Operé

Hysterosalpinography: direct measurement of gonadal radiation dose to the patient and the estimation of the probability of consequent stochastic radiation effects, by N. E. Tomlinson and R. M. Darwood

Problems and complications associated with percutaneous bile-duct drainage and endoprosthesis placement, by C. Williams and A. H. Chapman

ADAPTATION OF THE BLOMFIELD APPLICATOR FOR USE WITH THE SELECTRON

H. J. Appleby, H. Eckert and T. J. Godden

Departments of Radiotherapy and Medical Physics, Bristol Radiotherapy and Oncology Centre

The Blomfield applicator has been used by many radiotherapists for the past 25 years. The applicator has the advantage of providing rectal shielding, if required, allowing positional flexibility between the vaginal and uterine sources, and providing a system which is not dependent upon packing. To retain these advantages an adaptation to the Blomfield applicator has been developed for use with the Selectron. Details of the design and typical dose distributions around the applicator are demonstrated.

ENERGY RESPONSE OF FILM/SCREEN COMBINATIONS

M. Arnold, P. Liepins and N. E. Tomlinson

Guy's Hospital and Medical School, London

The major components for assessment of the radiographic process are the film/screen combination and the chemistry by which the film is to be processed. A wide variety of such systems is available, some designed specifically for a particular examination, *e.g.* mammography, whilst others are general purpose. The speed and latitude of the system chosen will affect the dose to the patient and the contrast present in the final image.

Because many fluorescent materials are used in intensifying screens, a range of responses for differing photon energies might be expected. Little work has been published on characterisation of film/screen systems over a range of energies (Vyborny et al, 1977; Venema, 1979; Kodera et al, 1984) and such information is rapidly outdated by the arrival of new "improved" screens. There is clearly a need for a standard method whereby the energy response of combinations of these imaging components may be reproducibly quantified. This would be useful not only in selecting the right combinations for a given technique, but also in the correct adjustment of automatic radiographic systems which often give the same exposure at all kVs selected, thus falsely suggesting no variation of response with energy.

A number of test X-ray spectra were used to expose the film/screen combinations, each having a very narrow range of photon energies. These were produced by heavy filtration of the beam with either copper or tin and molybdenum K-edge filters. The spectra used were measured by means of a high-resolution, solid-state germanium detector linked to a multichannel analyser. Direct spectral analysis was only possible at several metres from the tube and was reinforced by the attenuation of the filters in use. The amount of copper filtration was varied until a spectrum with a full width half maximum of 10 keV was obtained. In order to produce characteristic curves, the film was exposed progressively in steps using a specially designed mask and slider, which eliminated unwanted scatter and penumbra. A step-wedge was not used, as the variation of beam hardening with step thickness would alter the energy distribution of the photons incident on the film. Radiation exposures to the cassette were measured so that film speeds could be quoted in absolute rather than relative terms.

The findings to date show that film speed varies with energy. The effect of the film cassette and possibly optical wave-length shifters in the screens would make such results very difficult to predict theoretically. It is possible that enhanced radiographic efficiency could be achieved by matching the energy response of the imaging system to the X-ray spectra from the subject.

REFERENCES

KODERA, Y., DOI, K. & CHAN, H. P., 1984. Absolute speeds of screen-film systems and their absorbed-energy constants. *Radiology, 151*, 229–235.

VENEMA, H. W., 1979. X-ray absorption, speed and luminescence efficiency of rare earth and other intensifying screens. *Radiology, 130*, 765–771.

VYBORNY, C. J., METZ, C. E. & DOI, K., 1977. Screen/film system speed: its dependence on X-ray energy. *Radiology, 125*, 811–816.

THE *IN VITRO* ECHOGRAPHIC APPEARANCES OF GASTRIC WALL

J. Beynon, *D. M. A. Foy, †L. N. Temple, N. J. McC. Mortensen and ‡J. P. Virjee

*Departments of Surgery, *Medical Physics, †Pathology and ‡Radiology, Bristol Royal Infirmary*

The echographic appearances of the stomach wall have been investigated *in vitro* on freshly resected operative specimens. Delineation of the ultrasonic anatomy is essential for the interpretation of sonographic images obtained during endoscopic ultrasound examinations.

Specimens of normal stomach have been suspended vertically in a saline bath and scanned using an ultrasound scanner type 1846 (Bruel and Kjaer, Denmark) with 5.5 MHz and 7.0 MHz transducers. A five-layered ultrasonic image was consistently observed. Removal of the layers and subsequent histological examination has shown that the first (echogenic) layer corresponds to mucosa, the second (echopoor) layer to the muscularis mucosae, the third (echogenic) layer to submucosa, the fourth (echopoor) layer to muscularis propria and the fifth (echogenic) layer to serosa/fat.

With the growing interest in endoscopic ultrasonography, the correct delineation of the ultrasonic anatomy is imperative for the correct assessment of local invasion in malignant gastric neoplasms.

STAGING OF RECTAL CANCER BY ENDOLUMINAL ULTRASOUND

J. Beynon, A. Roe, *D. M. A. Foy, †L. N. Temple, N. J. McC. Mortensen and ‡J. P. Virjee

*Departments of Surgery, *Medical Physics, †Pathology and ‡Radiology, Bristol Royal Infirmary*

Five distinct ultrasonic layers have been identified in normal rectum and colon, both *in vitro* and *in vivo*, using an ultrasound scanner type 1846 (Bruel and Kjaer, Denmark) with 5.5 MHz and 7.0 MHz transducers.

The first (echogenic) layer corresponds to the mucosa, the second (echopoor) layer to muscularis mucosae, the third (echogenic) layer to submucosa, the fourth (echopoor) layer to muscularis propria and the fifth (echogenic) layer to the serosa/para-rectal fat. Occasionally a thin, incomplete, echogenic layer has been observed separating the two parts of the muscularis propria layer in the rectum. Assessments of 42 histologically proven rectal carcinomas have also been performed and results compared with histopathological findings in 37 cases and laparotomy observations in three cases. The coefficient of correlation between sonographic and histopathological findings was 0.92 ($P < 0.001$). Invasion beyond the muscularis propria was predicted with a sensitivity of 96% and specificity of 92% and had a predictive value of 96%. Lymph-node involvement was predicted in 17 cases. Correlation with histopathology revealed the technique to have a sensitivity of 92% and specificity of 73% and predictive value of 65%.

Endoluminal ultrasound staging of rectal cancer is more accurate than digital evaluation and its use pre-operatively aids the planning of subsequent treatment.

INHERENT FILTRATION AS A FUNCTION OF BEAM ANGLE FOR DIAGNOSTIC X-RAY TUBES

R. Bovill and R. W. Cranage

Department of Medical Physics, Musgrove Park Hospital, Taunton

It has been recognised for some time that the inherent filtration of diagnostic X-ray tubes will vary with the angle of beam production along the anode—cathode axis. With the advent of digital image capture and processing techniques, some of which involve dual energy subtraction, this change in filtration across the X-ray beam could have a significant effect on the processed image. This effect is more pronounced in modern tubes with a 12° or 13° anode angle. We have therefore measured the variation in inherent filtration across a number of tubes for a range of kVps and have attempted to fit the results with the standard theories of X-ray production from diagnostic targets.

A GRAPHICAL DOSIMETRY METHOD FOR "PARIS" BRACHYTHERAPY IMPLANTS

M. P. Casebow

Department of Medical Physics & Biomedical Engineering, Plymouth General Hospital

In the "Paris" system, the treatment volume is implanted with an array of parallel, equally spaced, linear radioactive sources of the same linear activity. It was developed about 20 years ago to facilitate the use of "afterloaded" ^{192}Ir wires, where the treatment dose was specified for an isodose surface, defined in relation to the "basal" dose-rate within the implanted volume. By contrast, the well known "Manchester" dosimetry system specifies the dose delivered at a given distance outside the implanted volume, and so cannot be used for dosimetry calculations with "Paris" implants.

Two main questions arise in practical brachytherapy calculations: how much radioactive material is required? and how is it to be distributed? For equally spaced arrays, both questions are answered rapidly and accurately using standard graphs and a few simple arithmetic calculations. The graphs have been plotted for linear, square and triangular arrays of parallel ^{192}Ir sources, and cover the wide range of implant sizes likely to be encountered in clinical use.

POST-IRRADIATION SURVIVAL OF DNA SYNTHESIS IN CYTOCHALASIN-TREATED CHINESE HAMSTER OVARY CELLS. A FLOW CYTOMETRIC METHOD

J. B. Court, C. Burn and J. L. Moore

Radiation Sciences Laboratory, Velindre Hospital, Cardiff

The fungal metabolite cytochalasin B blocks cytokinesis in cultured cells and results in an accumulation of DNA as cells become multinucleate We have previously shown (Court & Moore, 1985) that the post-irradiation survival of DNA synthesis can be monitored using Feulgen microdensitometry in cells cultured in the presence of cytochalasin B This provides an opportunity for a measure related to clonogenicity to be made on cells that are not monodispersed We have developed a method that uses flow cytometry to detect and enumerate surviving cells Following radiation exposure and incubation with cytochalasin, cells are detached from the culture flask using trypsin They are fixed by the direct addition of glutaraldehyde and the DNA content is measured in the flow cytometer following staining with mithramycin or chromomycin. Cells per sample are enumerable absolutely, by means of a known number of non-fluorescent polystyrene beads added with the trypsin and detected using forward scatter. The technique has been used to investigate the properties of the cytochalasin-based survival assay

REFERENCE

COURT, J. B. & MOORE, J L, 1985 The survival of cytochalasin-induced multinucleation following irradiation of Chinese hamster ovary cells *Cell Biology International Reports*, *9*, 219–227

DETERMINATION OF X-RAY SPECTRA FROM MEASUREMENTS OF ATTENUATION

D. R. Dance

Physics Department, The Royal Marsden Hospital, London

Detailed knowledge of X-ray spectra is required for the computer modelling and optimisation of X-ray imaging systems The measurement of these spectra requires expensive equipment and is often not practicable within the X-ray department. We have developed a method of estimating spectra from measurements of narrow beam attenuation The measurements are fitted using sets of standard spectra which can be adjusted by computer (filtration(s) and potential) until good agreement is reached between measured and calculated attenuation coefficients The method has been used for mammographic X-ray spectra from both molybdenum and tungsten targets with and without K-edge filters, and excellent fits have been obtained in all cases. The precision and limitations of the technique will be discussed

K-EDGE FILTERS AND MAMMOGRAPHY

D R. Dance, R. Davis, S. H Evans, C. H. Jones and C A. Parsons

Departments of Physics and Radiology, The Royal Marsden Hospital, London

The choice of X-ray spectrum for mammography is a compromise between the requirements of good image quality and low radiation dose to the breast. Various workers (including our own group) have pointed out that the X-ray spectrum obtained with a molybdenum target/molybdenum filter combination is too low in energy for optimal imaging of the thicker breast We have investigated the use of various K-edge filters to modify the X-ray spectrum, and the effects of these filters are presented in terms of calculations of contrast, dose, and noise for images obtained using a film/screen system The calculations are supplemented with an assessment using breast phantoms and specimen radiography with the Xerox 120 system. The benefits of using a mammographic grid are stressed

COMPUTED TOMOGRAPHY-GUIDED CANNULA INSERTION IN PELVIC HYPERTHERMIA

G. C. W. Howard, *A. K. Dixon and N. M. Bleehen

*Medical Research Council Unit, University Department of Clinical Oncology and Radiotherapeutics and *University Department of Radiology, The Clinical School, Cambridge*

Hyperthermia has been demonstrated to be a useful modality in the treatment of cancer, particularly when combined with radiotherapy. Temperatures across a heated volume are known to vary considerably and intratumour measurements are essential For superficial lesions this is not usually a problem, but in the regional heating of deep-seated tumours, placement of temperature measuring devices can be difficult. We have used thermistors to measure temperatures during the regional heating of extensive pelvic tumours The thermistors are placed down blind-ended cannulae inserted into the tumour. In six patients these cannulae have been inserted under CT-scan control Following confirmation of a normal platelet count and normal coagulation, limited CT cuts of the tumour are performed to locate the most suitable area for insertion. The skin is infiltrated with local anaesthetic and the needle used as a guide to the direction of insertion The desired depth is measured on the scan and the cannula inserted accordingly within an introducer. The exact position is confirmed on the scanner and a hard-copy record obtained In this manner cannulae have been inserted into six patients to depths of up to 10 cm, two with presacral rectal tumour recurrences, performed prone, two with bladder tumours, and one each with a prostatic carcinoma and a pelvic sarcoma, performed supine This procedure, usually completed within 30 min, is well tolerated and to date there have been no complications During hyperthermia treatments, a thermistor probe can be tracked along the cannula to record a temperature profile

We consider that this is a useful, safe, and quick procedure and, when possible, is of great value in pelvic hyperthermia

TECHNIQUES FOR INTRAORAL ELECTRON TREATMENTS

F. R. Hudson, M. Samarasekara and D. Hynd

Physics Department, Mount Vernon Hospital, Northwood, Middlesex

A new technique for the positioning of intraoral electron applicators is demonstrated It is shown that the applicator can be securely mounted on an external shell to provide positive location and to eliminate the problem of matching the treatment machine to an unstable and vulnerable target in the mouth

THE WHO BASIC RADIOGRAPHIC SYSTEM: AN EVALUATION OF TWO UNITS FOR USE IN A NHS DISTRICT HOSPITAL

G. de Lacey, A. Paris and J. Detain

Northwick Park Hospital and Clinical Research Centre, Middlesex

The basic radiographic system (BRS) has been developed by the WHO as an imaginative answer to the need for a simple, low maintainance X-ray unit for primary health care in the Third World. Several manufacturers now produce units designed to meet the WHO specifications for a fixed source-to-cassette geometry of 90° and 140 cm. Two of these, the Siemens Vertix B and the Todd Research BRS (modified to use 30 kW and 24 kW generators, respectively, and with a light beam diaphragm) have been assessed to define the advantages/disadvantages of such units in the NHS. In excess of 2500 patient examinations have been completed. We report some findings.

BRS acceptability by the radiographers varied greatly. In casualty, 34% of patients could not be examined at all or only with great difficulty; the figure for inpatients was 19% and for outpatients 6%. Regarding image quality as assessed by the radiologists, the Siemens unit was as good as conventional equipment, though the Todd unit was regarded as acceptable only. Chest radiography was popular among radiographers and radiologists alike, due to the ready centred unit and use of high kV technique with a fine grid. Some projections were impossible on both units, (*e g.* axial shoulder, lateral neck of femur). The BRS trolleys were not liked; being low they cannot be used without bending the back and they are difficult to manoeuvre. The BRS is not compatible for use with casualty trolleys or beds.

Data collection is not yet complete, but reports will be available in the autumn.

ASSESSING ABNORMAL LIVER BIOCHEMISTRY: WEDGE HEPATIC VENOGRAPHY? LIVER BIOPSY? WEDGE HEPATIC VENOUS PRESSURE?

D. J van Leeuwen, P. Scheuer, S. Sherlock and R. Dick

Departments of Medicine, Histopathology, Surgery and Radiology, Royal Free Hospital and School of Medicine, London

Biochemical screening of patients with suspected liver disease often reveals abnormalities, though the severity of liver disease may not be reflected clinically or biochemically. Liver biopsy is unpleasant and has a morbidity. Forty-nine patients had liver biopsy and also wedged hepatic venography and pressure studies. The appearance of the hepatic vein radicles at venography, the corrected hepatic venous pressures and the histological changes on biopsy were all categorised and compared by independent observers The radiological studies proved a reliable alternative to biopsy, whilst a corrected pressure (WHVP − FHVP) gradient of over 5 mmHg always indicated significant liver disease

TUMOUR MARKERS IN MALIGNANT TERATOMA: RESULTS FROM A STUDY IN THE SOUTH-WEST OF ENGLAND

P. A. Light and S E. Goodman

Bristol Radiotherapy and Oncology Centre

The South-west Testicular Tumour Study Group was established in 1981, incorporating its own facility to measure the markers alpha-fetoprotein (AFP) and human chorionic gonadotrophin (HCG) in serum samples from testicular teratoma patients within the Region Of the 134 patients registered into the study group, 71 were apparently clear of disease following orchidectomy. (Results from these patients will be presented during this meeting). The remaining 63 patients were found to have spread of disease beyond the removed testis and received further treatment. Marker values from individual cases from this group will be described, to illustrate various aspects of the role of marker measurements in the management of testicular teratoma patients.

REAL-TIME OCULAR ULTRASOUND IN THE MANAGEMENT OF MALIGNANT MELANOMA OF THE CHOROID

N C. McMillan

Department of Radiology, Western Infirmary, Glasgow

Real-time ultrasound now has an undisputed place in the early management of malignant melanoma of the choroid. As well as confirming the presence of a solid tumour, it is a very accurate method of obtaining its dimensions and assessing its position relative to the optic disc. This information is of critical importance in the choice of treatment. Present ophthalmic trends are away from enucleation, with local excision of the tumour now established as an effective method of treatment in experienced hands. Ultrasound is frequently the only method of imaging the eye post-operatively and some associated complications are described Other main treatment options are local radiotherapy by ruthenium-106 plaque or laser photocoagulation The accuracy of the plaque position can be determined ultrasonically while changes in tumour size can be documented on serial follow-up.

Extraocular extension of tumour, although recognised, has been a rare occurrence in our experience This paper reflects our practice of real-time ocular ultrasound gained from experience of over 70 cases of choroidal melanoma referred to the Western Infirmary, Glasgow in the past 2 years

CINE COMPUTED TOMOGRAPHY-DERIVED LEFT VENTRICULAR EJECTION FRACTION USING A SINGLE CENTRAL SLICE

R. M MacMillan, M. R. Rees and D. L. Clark

Killingbeck Hospital, Leeds

Cine computed tomography (cine CT)-derived left ventricular ejection fraction (LVEF) using a long-axis view has been validated by cardiac catheterisation (MacMillan et al, 1985). This method requires imaging of the entire left ventricular (LV) cavity, selection of end-systolic and end-diastolic frames and measurement of volumes of each slice Using Simpson's rule, LVEF can be calculated. The objective of this research was to develop a reliable and less time-consuming method for measuring LVEF. Twenty patients (nine female), mean age 60 (range 27–78) years, were studied. Cine CT LVEF was determined by Simpson's rule using the long-axis scan projection, LVEF was then measured by selecting the end-diastolic image with the largest cavity area. The corresponding end-systolic cavity area was measured. Apex-to-base distance was measured for each image Using the standard formula for measurement of LVEF by single-plane ventriculography, LVEF was obtained for each patient. A significant correlation was found between the Simpson's rule-derived LVEF and the single-slice method ($r = 0.97$; $p < 0.1$). We conclude that the single-slice method for determination of LVEF using a long-axis view is both easy to obtain and reliable Since cine CT is relatively non-invasive, easily repeatable and can be carried out on an outpatient basis, this technique represents a significant advance in the non-invasive approach to cardiac investigation

REFERENCE

MacMillan, R. M., Rees, M. R., Maranhao, V. & Clark, D. L., 1985 Comparison of left ventricular ejection fraction by cine computed tomography and single plane right anterior oblique ventriculography *Angiology*, *36*, 587–588.

A COMPUTED TOMOGRAPHY SCANNER PHANTOM FOR CHECKING ELECTRON DENSITY AND DISTANCE MEASUREMENTS ON A TREATMENT PLANNING COMPUTER

A. K Morgan, D. H. Temperton, R. G. Putney and S. C. Klevenhagen

Department of Medical Physics, The London Hospital

Data from a CT scanner (*e.g* body contours, densities of anatomical structures) can be used by a treatment planning system when calculating an isodose distribution. Computed tomography density information is expressed in the form of X-ray attenuation coefficients or Hounsfield units The treatment planning system converts the CT-density information to electron-density data, which are used in the calculation of the isodose distribution.

A variation of CT number of 10–15%, or a variation of tissue depth of 3–5 mm, can alter the resulting dose distribution by 1–2%. The ability of a CT scanner consistently to calculate CT number and tissue thicknesses should, therefore, be evaluated before using electron-density data from a CT scan for treatment planning One method of doing this is to scan a phantom of different-density materials and measure the CT numbers calculated by the scanner The phantom used for this is made from epoxy resin-based tissue-equivalent materials and has 1 mm holes drilled in it so that spatial accuracy can also be checked. Measurements are performed weekly and after any major service or repair to the CT scanner. This poster describes the phantom and the quality assurance protocol and discusses the results obtained

A HIGH-POWER PULSED DYE LASER FOR DYNAMIC PHOTOTHERAPY OF TUMOURS

A. W. Preece, N. P. Luckman and D. H. Follett

Radiotherapy and Oncology Centre, Bristol

Dynamic phototherapy involves the intracellular activation of haematoporphyrin complexes (HPD) to release cytotoxic singlet oxygen radicles. Light of a wavelength coincident with an absorption peak is used to activate the HPD, using a lower-frequency peak to ensure adequate light penetration of tissue A tunable dye laser is described which provides adequate light for tumour illumination, but which is of sufficient efficiency to operate on single phase outlets with minimal cooling requirements.

Light from a linear xenon flashtube is concentrated with an elliptical aluminium mirror into a parallel dye cell which contains a circulating solution of the organic dye Rhodamine B in methanol. Laser action occurs for pulsed light with a fast rise time (1 μs) and pulse duration of 10 μs. The resonator consists of a partially reflecting dielectric mirror and a reflecting diffraction grating (operating in the Littrow arrangement) which selects the wavelength of interest. The laser light is transmitted along optical fibres to the treatment site. The flash capacitor supply uses a novel voltage multiplying resonant circuit to obtain 1 6–2 kV from mains voltage without using transformers. Discharge is by fast-switching thyristors and a simmer supply improves discharge uniformity and lamp life.

COMPUTED TOMOGRAPHY DOSE AND IMAGE EVALUATION USING IONISATION CHAMBERS AND TEST OBJECTS MADE AT THE LONDON HOSPITAL

R. Putney, S. Dye and D. Temperton

Department of Medical Physics, The London Hospital, Whitechapel

"It seems very likely that computerised tomography (CT) now makes a major contribution to the collective population dose from diagnostic radiology in many developed countries" (NRPB-R173) A detailed knowledge of the performance of CT machines enables patient dose to be kept to the minimum. Dose measurements (thermoluminescent) are tedious because of the large number of dosemeters required. An ionisation chamber-based system can measure CT dose quickly and easily, providing information on the dose profile, slice overlap and multislice dose.

Ionisation chambers were built based on the design of J. Poletti but the geometry construction and chamber materials were altered Improved resolution allowed slice widths down to 4 mm to be measured Test objects have been made that measure resolution, noise, geometric distortion, slice thickness, linearity and the effective energy of the radiation beam. The test objects (except noise and resolution) are embedded in or consist of epoxy resin material and are, therefore, very stable and durable. The linearity of CT number (HU) with attenuation coefficient and electron density can be determined in the range from air to bone in regular increments More detailed data in the soft-tissue range can be obtained using a further set of test objects having equal increments of 20 HU. Using these test objects, a complete set of performance measurements can quickly be obtained Typical results are presented for two modern CT machines a Philips 350 Tomoscan and an IGE 9000 Series 1.

THE INFLUENCE OF TIME OF DAY OF ADMINISTRATION OF VAC CHEMOTHERAPY ON MYELOSUPPRESSION, SEQUENTIAL SERUM URATE AND THE CIRCADIAN RHYTHM OF URATE EXCRETION

M. H. Robinson, *R. Pownall and *M. S. Knapp

*Department of Radiotherapy, Churchill Hospital, Oxford and *Department of Medical Information Technology, University Hospital Nottingham*

The toxicity in animals of many cytotoxic agents has been shown to vary with the time of day of administration. Recently this has been demonstrated in humans treated with cisplatinum and Adriamycin Urate excretion by the kidney follows a significant circadian pattern in normals Significant rises occur following some anticancer therapy which may be related to cell kill

A prospective randomised study of the influence of the time of day of administration of the first course of vincristine

(2 mg), Adriamycin (40 mg/m^2) and cyclophosphamide (1 mg/m^2) (VAC) on its myelotoxicity and on the changes in serum and urinary urate rhythms was carried out in 21 patients with small cell lung cancer. Drugs were given at either 0900 or 2100. A significantly greater fall in total white cell count and neutrophil count had occurred 1 week after chemotherapy in the 0900 treated group compared with those treated at 2100 ($P < 0.05$). This difference was not apparent 2 and 3 weeks post-treatment. No differential effect on platelet count occurred. A significant transient rise in serum urate occurred between days 0 and 2 post-treatment in both groups ($P < 0.01$). No consistent rhythm in the excretion of urine or its urate content was demonstrated in any patient. Significant changes in urate excretion following chemotherapy occurred in all patients without any clear overall pattern being apparent. Thus this study suggests that the time of administration of VAC may influence its toxicity.

THALLIUM-201 MYOCARDIAL SCINTIGRAPHY AFTER VOLUNTARY HYPERVENTILATION

J. Teijeiro-Vidal, A. Mateo, M. J. Perez-Castejon,
F. Garcia and E. Operé

University Hospital Clinic, Zaragoza, Spain

Myocardial uptake of ^{201}Tl was evaluated in 18 healthy young volunteers, after 3 min of voluntary hyperventilation, 10 min after radionuclide injection and again 2 h later. The images were processed and stored in a computer, and the results expressed in a quantitative mode. The following parameters were analysed: total myocardium, intraventricular septum, left ventricular free wall, lung and liver uptake, as well as the myocardium/lung (TM/L) and myocardium/liver (TM/LV) ratios, in order to know the relative radionuclide uptake. The presence of respiratory alkalosis after hyperventilation (HV) was corroborated, with a significant decrease in pCO$_2$ and bicarbonate and increased pH in capillary blood. Early myocardial uptake, although uniform, was very poor, becoming normal 2 h later.

The hyperventilation results were alkaline values for pH (7.54 ± 0.04), decreased pCO$_2$ (26.6 ± 4.97 mmHg) and CO$_3$H$^-$ (20.2 ± 4.08 mEq/l). These results were very different from those obtained 2 h later (7.40 ± 0.05, 35.4 ± 5.11, and 27.7 ± 1.64 respectively) and statistically significant. The TM/L and TM/LV ratios obtained after HV were lower and myocardial uptake was uniformly diminished. Two hours later we observed significantly higher TM/L and TM/LV ratios due to an increased myocardial uptake. No decrease of activity was observed in lungs and liver. Myocardial activity was significantly increased.

HYSTEROSALPINGOGRAPHY: DIRECT MEASUREMENT OF GONADAL RADIATION DOSE TO THE PATIENT AND THE ESTIMATION OF THE PROBABILITY OF CONSEQUENT STOCHASTIC RADIATION EFFECTS

N. E. Tomlinson and R. M. Darwood

Department of Clinical Physics and Bioengineering, Guy's Hospital, London

One couple in 10 present for the investigation of infertility. The recent high incidence of pelvic inflammatory disease and the modern trend toward pregnancy late in the reproductive careers of women have created a substantial demand for examinations of tubal patency. Essentially, two alternatives exist; hysterosalpingography (HSG) and laporoscopic techniques.

At Guy's Hospital, a new balloon-catheter HSG method has been introduced. In order better to evaluate the merits of such a technique, a dosimetry study was conducted. A sophisticated applicator was designed and constructed so that a pair of thermoluminescent dosemeters (TLDs) could be inserted per vaginam and positioned at the internal os, thus being adjacent to the ovaries.

Dosimetry studies were conducted as a routine part of indicated HSG examinations on 21 women. Great care was taken to ensure that the TLDs remained within the field-of-view throughout all fluoroscopic and radiographic exposures.

The average absorbed organ dose to the ovaries was found to be about 1.9 mGy with a range from 5.2×10^{-1} to 6.9 mGy. Adopting the ICRP philosophy (ICRP, 1977), the mean average excess risk of hereditary defects in the descendants of the irradiated individuals was calculated as about 1.9×10^{-5} (1 : 52000). This value should be compared with a risk of such defects from "natural causes" of 3×10^{-2} (H.A.L.H.B.S., 1977).

The work has been further extended to cover the estimation of whole-body dose equivalents to the patient by the application of data and methods from a Monte-Carlo dosimetry model originated by Kereiakas and Rosenstein (1980).

The calculations indicate a mean average whole-body dose equivalent of about 0.6 mSv with a range from 0.15 to 2.2 mSv. These values of dose may be used in the calculation of the total risk of patient mortality from radiation-induced cancer, again using the ICRP philosophy. The mean average risk value for this study was about 6.0×10^{-6} with a range from 1.6×10^{-6} to 2.2×10^{-5}.

Taken together, the results of this study indicate that considerations of radiation-induced cancers and abnormalities are of little significance when HSG is compared with other invasive techniques used to investigate tubal patency.

REFERENCES

ICRP, 1977. Recommendations of the International Comission on Radiological Protection. ICRP (26). Annals of ICRP, 1.

H.A.L.H.B.S., 1977. Frequency of genetic disease. A Monograph of the National Institute of Child Health and Human Development, (Raven Press, New York).

KEREIAKAS & ROSENSTEIN, 1980. *Handbook of Radiation Doses in Nuclear Medicine and Diagnostic X-ray.* (CRC Press)

PROBLEMS AND COMPLICATIONS ASSOCIATED WITH PERCUTANEOUS BILE-DUCT DRAINAGE AND ENDOPROSTHESIS PLACEMENT

C. Williams and A. H. Chapman

St James's University Hospital, Leeds

Percutaneous biliary drainage has become a frequently performed procedure, and although drains and stents can be placed with an endoscope, high duct obstructions generally still require the percutaneous approach. Percutaneous biliary drainage was performed in 100 patients with malignant bile-duct obstruction considered inoperable or unfit for surgery. Internal/external drainage (30 patients) was performed using a Ring 8.3 French catheter (Ring et al, 1979). Early complications (within 30 days) were encountered in 16 of the patients; cholangitis and septicaemia (14), renal failure (three), biliary peritonitis secondary to catheter displacement (two), haemobilia (two), dehydration and electrolyte imbalance (two), subphrenic abscess (one), catheter leakage (one), and skin granuloma (one). Early complications were encountered in 12 of the 70 patients undergoing endoprosthesis placement (Coons & Carey, 1983); cholangitis and septicaemia (nine), renal failure (two), haemobilia (three), duodenal haemorrhage (one) and duodenal perforation (one). Late recurrent biliary obstruction was usually caused by endoprosthesis migration or tumour blocking the endoprosthesis. In 8% of the patients the lesions could not be crossed and the patient had to be left on external drainage. Improved patient acceptance and the reduced complication rate explains our preference for endoprosthesis placement. Methods of reducing the number of complications and overcoming the problems associated with biliary drainage are described and illustrated.

REFERENCES

COONS, H. G. & CAREY, P. H., 1983. Large-bore, long biliary endoprosthesis (biliary stents) for improved drainage. *Radiology, 148,* 89.

RING, E. J., HUSTED, J. W., OLEAGA, J. A. & FREEMAN, D. B., 1979. A multihole catheter for maintaining longterm percutaneous antegrade biliary drainage. *Radiology, 132,* 752–754.

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Radionuclide research fellowship

The Patrick Grove Memorial Fellowship
Amersham International plc have funded this fellowship, for research into diagnostic or therapeutic work with radionuclides, through the Radiological Research Trust, to encourage young men and women to pursue original work in the United Kingdom.

Applications are invited from heads of departments and others in appropriate administrative positions in the UK, or from individuals world-wide (who should enclose a supporting letter from the UK department in which they wish to work).

The application should include a full curriculum vitae of the candidate, who should be a clinical or non-clinical medical graduate. It should state the purpose, background and plan of investigation of the projected research and explain how this would fit into existing and projected departmental work. The initial fellowship is for three years and will cover salary in the region of £15 000 p.a., together with modest departmental expenses.

For further information please contact: Professor G. H. du Boulay C.B.E., The Radiological Research Trust, 36 Portland Place, London W1N 3DG. *The closing date is September 1, 1986.*

Report of the 1986 Vienna Meeting of the ICRP

The International Commission on Radiological Protection (ICRP) met in Vienna, Austria, April 20–24, 1986. One report, "The metabolism of plutonium and related elements", was adopted and will be published in *Annals of the ICRP* in 1986. Two other reports, "Developmental effects of irradiation on the brain of the embryo and fetus" and "Lung cancer risk from indoor exposures to radon daughters" were reviewed in detail and are likely to be adopted by the Commission during 1986. Initial consideration was also given to a further report, "Radiation dose to patients from radiopharmaceuticals", which is likely to come before the Commission for adoption in early 1987.

There was a general discussion of policy issues which will need to be considered by the Commission and its expert committees as a background to any eventual revision of the Commission's recommendations. A comprehensive catalogue of such policy issues was developed with the individual items to be discussed in detail by the Commission and its committees at their future meetings.

Reduced rate hotel accommodation

Expotel have agreed to provide reduced rate hotel accommodation for members of the BIR who wish to stay overnight in London. Please contact Expotel, not the BIR, for all booking information and arrangements, on one of these telephone numbers: London office 01-568 8765, Manchester office 061-431 8000, or Glasgow office 041-221 8700.

Notices

Presidential promotion

Congratulations to the BIR President, P. N. T. Wells, who was appointed Honorary Professor in Radiodiagnosis at the University of Bristol on August 1

IARC awards

International Agency for Research on Cancer, World Health Organization, Lyon, France

Fellowships for research training in cancer, 1987–1988

Applications for training fellowships in 1987–1988 are invited from junior scientists wishing to be trained in those aspects of cancer research related to the Agency's own programme epidemiology, biostatistics, environmental and viral carcinogenesis and mechanisms of carcinogenesis. Applicants should be engaged in research in medical or allied sciences and intend to pursue a career in cancer research. Applications cannot be accepted from people already holding fellowships enabling them to study abroad

Fellowships are normally awarded for one year and are tenable at the Agency or in another suitable institution abroad. Fellows will, in general, be selected from applicants with some postdoctoral research experience related to cancer in medicine or the natural sciences. Applicants requiring basic training in cancer epidemiology will also be considered They must have an adequate knowledge, both written and spoken, of the language of the country in which their fellowship is tenable.

Stipends will vary according to the cost of living in the country of study. The cost of travel for the applicant and, in certain circumstances, that of one dependent will be met

Visiting scientist award 1987–1988

This award (one per year) is intended for established cancer research workers, with a minimum of five years' postdoctoral experience, who wish to spend one year at IARC, working on the implementation of a collaborative research project related to the Agency's own programmes. epidemiology, biostatistics, environmental and viral carcinogenesis and mechanisms of carcinogenesis.

Applicants must belong to the staff of a university or a research institution. They must provide a written assurance that they will have a position to return to at the end of the period of award Candidates should submit their applications after consultation with an IARC scientific staff member. Applications will be reviewed by the Fellowships Selection Committee each year There will be an annual remuneration and the cost of travel will be met.

Fellowship application forms and more detailed information are available from Chairman of the Fellowships Selection Committee, International Agency for Research on Cancer, 150 cours Albert-Thomas, 69372 Lyon Cedex 08, France Applications must reach the Agency not later than December 31, 1986

New neuroradiology post

Dr Tim Jaspan, Senior Registrar in Radiology on the Nottingham/Derby training scheme, has been appointed as the first incumbent of a new post—The Merck Fellowship in Neuroradiology at the University Hospital in Nottingham

This post is designed to give further training and experience in neuroradiology to individuals holding the F.R.C.R who wish to specialise in this branch of radiology. The post offers experience with all forms of neuroradiological investigation including computed tomography, digital vascular imaging and magnetic resonance imaging.

As the title implies, this Fellowship has been endowed thanks to the generosity of Messrs E Merck Ltd.

Reference beta radiations for calibration purposes

BS 6689 *Specification for reference beta radiations for calibrating dosemeters and doseratemeters and for determining their response as a function of beta radiation energy* specifies requirements for reference beta radiations produced by radionuclide sources to be used for the calibration of protection level dosemeters and for the determination of their response as a function of beta energy. It gives the characteristics of such radionuclides and examples of suitable source constructions and describes methods for the measurement of the residual maximum beta energy and the absorbed dose-rate at a depth of 7 mg cm^{-2} in a semi-infinite tissue-equivalent medium. The energy range involved lies between 66 keV and 3.6 MeV and the absorbed dose-rates are in the range from about 10 $\mu Gy\ h^{-1}$ to at least 10 Gy h^{-1}. Two series of reference beta radiations are proposed from which the radiation necessary for determining the characteristics (calibration and energy response) of an instrument will be selected

The standard is identical to ISO 6980 published by the Internal Organization for Standardization (ISO) Copies of BS 6689 may be obtained from the Sales Department, British Standards Institution, Linford Wood, Milton Keynes MK14 6LE, price £16 50 (£6.60 to BSI subscribing members)

The Ionising Radiations (Fees for Approvals) Regulations 1986

The *Ionising Radiations Regulations 1985*, which came into operation on January 1, 1986, provided for the approval, by the Health and Safety Executive (HSE), of dosimetry services and of certain types of articles containing radioactive substances

Since it has been the policy of the Health and Safety Executive/Commission to make charges to recoup the cost of conferring such approvals, the *Ionising Radiations (Fees for Approvals) Regulations 1986* (SI No 1986/669), now published, contain the authority for these charges and the rates payable. These regulations came into force on May 6, 1986.

Information on how to apply for approval may be obtained from any Area Office of the HSE Other charges made by the HSE were contained in the *Health and Safety (Miscellaneous Fees) Regulations 1986*, which came into operation on April 1, 1986

The Ionising Radiations (Fees for Approvals) Regulations 1986, ISBN 0 11 066669 0 price £0 80 is available from HM Stationery Office or bookshops.

ICRU reports

The MRC Radiobiology Unit, Chilton, Didcot, Oxon, UK (Tel 0235-834393) is available as a source of supply of new reports from the International Commission on Radiation Units and Measurements

BIR calendar events

Unless otherwise indicated, enquiries about the following events should be addressed to the Assistant Secretary: Programme, British Institute of Radiology, 36 Portland Place, London W1N 3DG (Tel. 01-580 4085).

The meetings are at 36 Portland Place unless otherwise stated. Attendance is open to non-members.

Joint RCR/BIR/RSM Autumn Provincial Meeting; RCR Annual General Meeting
September 11–13, 1986
University of Sheffield
Organised by the RCR. Further details from the Meetings Secretary, The Royal College of Radiologists, 38 Portland Place, London W1N 3PG (Tel. 01-636 4432/3).

Regulations and Guidance on Radiation Protection: a seminar
October 2, 1986 at 10 a.m.
Middlesex Hospital Medical School, London W1
Chairmen: Professor R. J. Berry (morning session) and Mrs J. Barrett (afternoon session).
Speakers: Mr P. Beaver, Dr J. Gill, Mr R. Grix, Mr I. Hendra, Mr B. Godfrey, Mr P. Richardson, Mr B. Aves, Dr L. K. Harding, Dr P. Roberts and Dr J. G. Russel.
Joint BIR/COR meeting.

Interventional Radiology of the Spine
October 16, 1986 at 5.45 p.m.
Provisional speakers include: Dr D. J. Stoker, Dr B. E. Kendall, Dr W. I. McCall and Dr D. E. Colhoun.

Accelerated and Hyperfractionation: experimental and clinical
November 14, 1986 at 11 a.m.
Organised by the Radiobiology Subcommittee. To conclude with the Slivanus Thompson Memorial Lecture: "Tumour structure and cancer treatment" by Dr R. H. Thomlinson.

Diagnostic and Therapeutic Uses of Radioisotopes in Oncology
November 26, 1986 at 10.30 a.m.
All day meeting to be organised by Nuclear Medicine Subcommittee.
Chairmen: Professor R. J. Berry and Dr R. T. D. Oliver. Speakers to include: Dr J. Fogelman, Dr N. W. Garvie, Dr K. E. Britton, Dr M. Granowska, Dr A. Epenetos, Dr S. Clarke, Dr P. N. Plowman.

Uroradiology Update
January 15, 1987 at 5.45 p.m.
Chairman: Dr D. Rickards. Speakers: Dr D. Rickards, Dr J. Pemberton, Dr C. E. L. Freer, Mr G. Watson, Dr R. Johnson, Dr W. Lees, Professor D. J. Allison.
Joint BIR/RCR/RSM meeting.

Nuclear Magnetic Resonance Update
February 6, 1987
Joint BIR/RCR all day meeting.

Lung Studies with Radioisotopes
February 11, 1987
Joint IPSM/BIR (Nuclear Medicine Subcommittee) all day meeting to be organised by IPSM.

All day non-topic proffered papers meeting
February 13, 1987
Joint ARR/BIR (Radiobiology Subcommittee) meeting to be organised by the Association of Radiation Research.

PACS and Related Hard Copy Systems
February 25, 1987
Chairman: Professor I. Isherwood.
All day meeting to be organised by Industry Committee.

Radiology '87
April 1–3, 1987
University of Southampton
45th Annual Congress of The British Institute of Radiology.

The Finzi Lecture
April 15, 1987
Royal Society of Medicine, London
"The solitary pulmonary nodule" by Dr S. Segalmann.
Meeting to be organised by RSM.

Annual General Meeting
May 14, 1987 at 4.30 p.m.

Imaging in Radiotherapy
May 15, 1987
Chairmen: Dr D. Thwaites and another to be announced.
Joint IPSM/BIR all day meeting to be organised by IPSM.

Dysphagia
May 20, 1987
Royal Society of Medicine, London
Joint RSM/RCR/BIR all day meeting to be organised by the RSM.

Library news

The BIR Library is open weekdays 9 a.m.–5 p.m. (7 p.m. on Thursdays)

The Librarian, Mrs Gunnel Ingham, is in attendance Tuesdays 11 a.m.–5 p.m., and Thursdays 11 a.m.–7 p.m., and Mrs Angela Lansdown, daily 9 a.m.–5 p.m. (Tel. 01-580 4085).

The journal stock includes more than 100 titles. Though journals may not be taken out of the library, there is a photocopy service, also available by post. A list of current journals is available on request and is also published in the March and September issues of the Bulletin.

Most books (excepting the historical collection) are available on loan.

Recent additions to the Library

Berquist, T. H. (Ed.): Diagnostic imaging of the acutely injured patient. 1985
Davidson, A. J.: Radiology of the kidney. 1985
Levene, M. I., Williams, J. L. & Fawer, C.-L.: Ultrasound of the infant brain. 1985
Nyborg, W. S. & Ziskin, M. C. (Eds): Biological effects of ultrasound. 1985
Potten, C. S.: Radiation and skin. 1985
Prime, D.: Health physics aspects of the use of radioiodines. 1985
Steel, W. B. & Cochrane, W. J. (Eds): Gynecologic ultrasound. Clinics in diagnostic ultrasound. 15. 1984
Suit, H. D. & Proppe, K. H.: Soft tissue sarcomas. 1983

Press releases

Air courier service helps leukaemia victims

Airborne Express, an air courier company, is providing a vital service to victims of leukaemia and other blood disorders.

Bone marrow transplants organised through the Anthony Nolan Research Trust in London are now proving an effective treatment for many treated leukaemia sufferers diagnosed at an early stage. A major problem, however, is finding suitably matched donors which can only be done by checking donor profiles from many countries around the world. This is where the speed and efficiency of the Airborne Express service is vital; blood sample analyses, medical charts and patients' dossiers need to be sent to and from destinations all around the world, quickly and reliably.

According to Dr James, head of the Anthony Nolan laboratories in London, a typical case could involve a patient from Cologne, Germany, who will be operated on in Seattle, USA, using marrow from a donor in London. Around a quarter of leukaemia sufferers can find a suitable donor from within their own family, but for the others the detailed information carried around the world by Airborne Express remains their best hope.

Currently, there is no shortage of willing donors. In London, the Round Table Organisation holds donor clinics four evenings a week, at which blood samples are taken for analysis. The information produced is then stored on a computer and relevant details sent, on request, via air courier, to hospitals and clinics all over the world.

The Anthony Nolan Research Trust is named after a young Australian leukaemia sufferer who came to Britain in 1973 hoping to find a suitable donor for a bone marrow transplant. The boy's mother was told by Dr James that, given the lack of resources at that time, there was only one chance in 50 000 of finding a suitable donor fast enough. Mrs Nolan reacted by spending the next few years organising a high-profile fund raising campaign, and enough money was raised for Dr James to recruit four graduate researchers and buy essential laboratory equipment. The Trust now receives £5000 of government funding per year, although its operating costs are £250 000 and shortage of funds remains a major and increasing problem.

Donations (money, not marrow!) should be sent to: Anthony Nolan Research Trust, St Mary Abbotts Hospital, Marloes Road, Kensington, London W8.

Lead-loaded shielding putty

Reactor Experiments, Inc., announces the availability of Shield/Clay, a non-hardening, reusable, lead-loaded shielding putty for use in orthovoltage X-ray therapy. It is designed to permit an accurate, reproducible technique for obtaining small ports in shields moulded to fit the patient. Shield/Clay protects skin tissue surrounding the treatment area. The putty is pliable, yet has enough consistency to hold its shape after placement. It can be removed after application, stored and reused repeatedly. It has a density of 4.3 g/cm^3. The putty is the equivalent of one-third the same thickness of lead. The lead in Shield/Clay is evenly distributed throughout the material so there will be no "holes" apparent to the radiation.

For additional information and a free sample of Shield/Clay, please contact: Reactor Experiments, Inc., 963 Terminal Way, San Carlos, CA, USA 94070-3278, Telex No. 34 5505, or their UK representative, John Caunt Scientific Ltd, Oakfield Industrial Estate, Stanton Harcourt Road, Eynsham, Oxford OX8 1JA.

New IDIS-HS real-time DSA system from Quantel

To facilitate an even wider range of applications to be undertaken using DSA, Quantel have developed the new High-Speed IDIS, which provides real-time picture capture and is particularly useful for applications where high recording speeds are desirable.

This new high-speed addition to the IDIS family is capable of recording full resolution images at 6.25 images/s and reduced resolution images at 25 frames/s onto a high speed Winchester disk. Two versions of the disk are available, a standard 336 Mbyte disk providing over 3 min of recording, or the 672 Mbyte option which doubles the recording time. Real-time subtraction allows immediate visualisation of contrast medium during recording. Compactness and portability are maintained as both fit into the standard IDIS trolley. In addition to the comprehensive image processing and measurement package available on the standard IDIS system, the IDIS-HS offers the additional features of electrocardiographic gating, time interval differencing, colour-coded time of arrival and ventricularography.

IDIS is a totally British product designed, built and successfully marketed world-wide by Quantel. The power, flexibility and excellent diagnostic quality images of IDIS have been recognised throughout the world and reflected by the number of systems now in use.

For further information contact Susan Hayselden, Public Relations Officer, Quantel, Kenley House, Kenley Lane, Kenley, Surrey CR2 5YR (Tel. 01-668 4151).

Third generation DSA

The long-term experience of Kontron in general image processing has resulted in the MIPD digital radiography system which, apart from pure subtraction, applies complex algorithms in order to eliminate artefacts that are caused by patient movement. In addition, the filter algorithms for noise reduction and contour enhancement further improve the image quality. The array processor which is a standard feature in the MIP D enables complex procedures such as stenosis quantification and parametric images to be easily computed.

Due to the system's large 16 Mbyte semiconductor memory, it is possible to extend the application of the image processing system in the field of radiology to include the field of digital fluoroscopy as well. Data acquisition with a frequency of up to 50 images/s allows digital storage of motion sequences. The advantage of this technique is the display of any motion sequence over any period of time with the radiation switched off. This facilitates diagnosis and, moreover, results in a reduction of radiation exposure.

For further information, contact: Kontron Instruments, Medical Image Processing, Breslauer Str. 2, 8057 Eching bei Muenchen (Tel. 089-31901 220).

Colour flow mapping for real-time imaging of cardiovascular blood flow

Colour flow mapping is now an upgrade to the Hewlett-Packard ultrasound systems HP77020AC and HP77020AR. It provides real-time imaging of cardiovascular blood flow and results in faster mapping of regurgitant lesions. The colour representation of blood is shown as a two-dimensional image with colours coded according to the direction and velocity of blood flow relative to the position of the transducer.

Clinical applications of colour flow mapping include characterisation of blood flow profiles and possible flow areas of vessels, rapid detection and localisation of abnormal flow, quantification of regurgitant jet areas and determination of stenotic jet angles for a more accurate CW Doppler quantification. Information not shown on two-dimensional and Doppler images, such as the flow pattern and velocity with which blood fills the ventricles, may be seen with colour and multiple lesions are easier to identify.

Hewlett-Packard's colour flow mapping technology has been incorporated into the HP77020 phased-array imaging system without compromising any of the existing features such as the two-dimensional image and Doppler quality, as well as the system's reliability and portability.

For further information please contact: Literature Section, Hewlett-Packard Ltd, Eskdale Road, Winnersh Triangle, Wokingham, Berkshire RG11 5DZ (Tel. 0734-696622).

Medical product development in central London

The South Bank Technopark, since opening in May 1985, has set up 17 development activities occupying about 60% of its available space. The Technopark, which is the largest in the country, has already recognised the need to expand and a new wing is now planned for completion by the end of 1987. An entirely new venture, the formation of the Medical Products Centre, has been started in space reserved within the existing Technopark. Enthusiastic support is being provided by leading technology and investment organisations in London. Effective collaboration has also been arranged with expert advisers in the Health Service. Hospitals, companies and individuals, with good proposals for new medical products, now have the possibility of gaining adequate facilities to carry out new product investigation, design, pre-production and market introduction, for which they may not have resources of their own, either in terms of space or technical, managerial and financial needs.

The Centre can offer: ample space in various unit sizes for development work, a location in the heart of London, shared business services to improve efficiency and reduce overheads, technical support from the South Bank Polytechnic (including library services, computing, machining, fabrication, printed circuit board construction, and measurement and testing), consultancy aid in design and evaluation of the developing product, assistance in product trials through the DHSS and the NHS, and identification of potential suitable manufacturing and marketing organisations.

To take advantage of this opportunity send, to the address below, a summary of the proposed development project giving relevant information about the facilities required and a possible time scale. All this will be treated entirely confidentially and will form the basis of negotiation for the necessary allocation of space and resources. Further information from: Derrick Patient, Consultant, Medical Products Centre, South Bank Technopark Ltd, 90 London Road, London SE1 6LN.

Range of Micro cast collimators for gamma cameras

Van Mullekom Nuclear Fields have introduced a considerable extension to their range of lead Micro cast collimators for scintillation gamma-camera systems for nuclear medical applications.

The new Micro cast collimators, which are manufactured by a unique casting process, have a higher mesh-number than the current types. The various models have hexagonal, triangular, square and round holes with diameters of 1.2 mm or more. The septa thickness (the amount of material between two adjacent holes) is very small, down to only 0.1 mm in the newest models. These thin septa were, in the past, only achievable with foil designs.

Van Mullekom offers collimators with a parallel, converging, diverging and parallel-diverging hole configuration. The range includes 7-pinhole collimators as well as single-slanthole and double-slanthole collimators. Depending on the model, the thickness of the collimator can vary from 16 mm to 100 mm. They are suitable for applications in the range from 70 keV to 511 keV. The standard types have an effective diameter between 250 mm and 530 mm. If the standard range does not include a given collimator for a specific application, models can be built to order and to a client's non-standard specifications.

The collimators and other lead products for nuclear medicine applications, such as lead castles, lead shields, etc. are produced and supplied by Van Mullekom Nuclear Fields B.V. in Vortum-Mullem, The Netherlands, and Van Mullekom Nuclear Fields (Australia) Pty Ltd in St Marys, New South Wales, Australia.

Erbium X-ray filters

Erbium X-ray filters, now available from Reactor Experiments, Inc., reduce patient dose by as much as 50% in many common diagnostic radiological techniques. The filters are designed to replace or augment existing aluminium filters. No decrease in radiographic image quality is experienced with the use of erbium X-ray filters.

Erbium, a member of the rare-earth group of the periodic table, absorbs the low energy X rays as well as those at the high energy end of the spectrum: erbium filters provide excellent transmission of those X rays which contribute to the radiographic image while filtering out those that would normally be absorbed in the body. The filters are available to fit all diagnostic X-ray machines, including dental machines. For further information and copies of selected technical references, please contact: Reactor Experiments, Inc., 963 Terminal Way, San Carlos, CA, USA 94070-3278, Telex No. 34 5505. Our UK representative is John Caunt Scientific Ltd, Oakfield Industrial Estate, Stanton Harcourt Road, Eynsham, Oxford OX8 1JA.

Responsibility for Philips radiation therapy business transferred to MEL, UK

MEL, the Philips Defence and Medical Systems Company in the UK, based in Crawley, Sussex and Philips Medical Systems Division (MSD) in Best, Holland have reached an agreement whereby the whole of the Philips radiation therapy business has become a business accountable product centre, based at MEL. This centralisation includes all of the marketing and technical operations aspects of the business world-wide. The new General Manager for Philips Medical Systems at MEL is Mr Phil Holder.

Meetings and courses

As a service to our readers, the title, date and place of meetings and contact address will be inserted free of charge: any additional information will be charged at £1.75 per printed line, per insertion. Please contact the Managing Editor.

Postgraduate Fellowship Chest Radiology
Continuing education
San Diego School of Medicine, California, USA
Further details Secretary to Dr P J. Friedman, Radiology Department, University Hospital, 225 Dickinson Street, San Diego, CA 92103, USA (Tel 619-294 6684)

Visiting Fellowships in Magnetic Resonance Imaging
Continuing education
UCSD Medical Center/AMI Magnetic Resonance Institute
Further details. Vicki Broughton, Dept of Radiology, UCSD Medical Center, 225 Dickinson St, San Diego, CA 92103, USA (Tel 619-294 3856)

The Christie Hospital Symposium on Three-Dimensional Imaging, Three Dimensional Planning and Update on Current Trials
November 7–8, 1986
Christie Hospital, Manchester
The fifth annual symposium will concentrate on three-dimensional imaging and three-dimensional therapy planning. There will also be an update on current trials at the hospital.

The course is intended for consultants but there will be a limited number of places for senior registrars and registrars

Further details Dr B. Hancock, Christie Hospital, Wilmslow Road, Withington, Manchester M20 9BX.

Advanced Seminar on Diagnostic Radiology Dosimetry
November 10–14, 1986
CEC Joint Research Center, Ispra, Italy
Further details. C. Maccia, Centre d'Etudes sur l'Evaluation de la Protection dans le domaine Nucleaire (CEPN), Boite Postale No. 48, 92260 Fontenay-aux-Roses, France (Tel 1 46 54 76 59)

XIVth Symposium of the French Association for Technical and Scientific Radiation Protection: radiation protection problems encountered in great developments of new techniques and technologies
November 26–28, 1986
Paris, France
Subjects: industrial irradiation, non-destructive controls, radioactive gauges, mixed oxide fuel in LWR's cycle, controlled nuclear fusion, underwater operations in nuclear plants, fast breeder reactors, radioactive transports and non-ionising techniques
Language. in French only.
Further details Secretariat GRA, SPR, CEN Saclay, 91191 Gif sur Yvette, France

18th Annual Meeting of the British Medical Ultrasound Society
December 16–18, 1986
University of Warwick, Coventry
Further details. Mr M. F. Docker, Ultrasound Dept, Birmingham Maternity Hospital, Birmingham B15 2TT

Advanced Seminars in Diagnostic Imaging
January 9–12, 1987
San Diego, California, USA
Further details: Ryals & Associates, PO Box 920113, Norcross, Ga 30092-0113, USA (Tel 404-641 9773)

Practical Approach to Duplex Imaging
January 22–24, 1987
San Diego, California, USA
Further details: Ryals & Associates, PO Box 920113, Norcross, GA 30092-0113, USA (Tel 404-641 9773)

Reactor Accidents: what Chernobyl has taught us
January 28, 1987
City Conference Centre, London
Further details: Professor J H Martin, Department of Medical Biophysics, Building 15, Park Wynd, University of Dundee, Dundee DD1 4HN.

Imaging Solutions to Clinical Problems
February 9–25, 1987
Aboard Royal Odyssey with a destination of Australia and New Zealand
Further details. Ryals & Associates, PO Box 920113, Norcross, GA 30092-0113, USA (Tel 404-641 9773)

Neuroradiology Update
March 2–5, 1987
San Diego, Califonia, USA
Further details: Ryals & Associates, PO Box 920113, Norcross, GA 30092-0113, USA (Tel. 404-641 9773)

Magnetic Resonance Imaging for Technologists: symposium and workshops
March 3–5, 1987
San Diego, California, USA
Further details Ryals & Associates, PO Box 920113, Norcross, GA 30092-0113, USA (Tel 404-641 9773).

Magnetic Resonance Imaging
March 3–6, 1987
San Diego, California, USA
Further details Ryals & Associates, PO Box 920113, Norcross, GA 30092-0113, USA (Tel 404-641 9773).

British Nuclear Medicine Society Annual Congress
April 12–15, 1987
Imperial College, London
Further details: Mrs A. Taylor, BNMS Conference Secretary, 22 Leinster Avenue, East Sheen, London SW14 7JP

7th Annual San Diego Residents' Radiology Review Course
April 19–25, 1987
San Diego, California, USA
Further details: Ryals & Associates, PO Box 920113, Norcross, GA 30092-0113, USA (Tel. 404-641 9773).

Euroson '87: 6th Congress of the European Federation of Societies for Ultrasound in Medicine and Biology
June 14–18, 1987
Finlandia Hall, Helsinki, Finland
Further details. Congress Bureau, PO Box 824, SF-00101 Helsinki, Finland.

1st Copenhagen Symposium on Uroradiology: imaging and interventional techniques
September 7–10, 1987
Herlev Hospital, University of Copenhagen, Denmark
Further details: Dr Henrik S. Thomsen, Department of Diagnostic Radiology 54E2, KAS Herlev, Herlev Ringvej, DK-2730 Herlev, Denmark.

3rd Annual Physics and Biology of Radiology
August 31–September 4, 1987
San Diego, California, USA
Further details. Ryals & Associates, PO Box 920113, Norcross, GA 30092-0113, USA (Tel 404-641 9773).

BIR Publications

Basic Clinical Ultrasound
Hylton B. Meire and Pat Farrant. 170pp. 99 ill. 1982 **£12.00**

Central Axis Depth Dose Data for Use in Radiotherapy
British Journal of Radiology Supplement 17. 1983 **£8.00**

Treatment Simulators
(Applications of Modern Technology in Radiotherapy)
British Journal of Radiology Supplement 16. Revised 1981 **£3.50**

Quality Assurance
Proceedings of a CEC/CRAD Scientific Symposium on
Criteria and Methods for Quality Assurance in Medical
X-Ray Diagnosis. Udine (Italy), April 1984.
British Journal of Radiology Supplement 18. 1985 **£16.00**

Orders to:
Publications Department,
The British Institute of Radiology,
36 Portland Place, London W1N 3DG **(Tel: 01-580 4085)**

British Journal of Radiology Supplement 19

Radiation Damage to Skin

Fundamentals and Practical Aspects

Proceedings of a Workshop held at Saclay, France, on October 9–11, 1985, organised by the Commission of the European Communities and the Commissariat à l'Energie Atomique de Protection et de Sûreté Nucléaire, Fontenay-aux-Roses, France.

Skin and underlying tissues are frequently critical structures in radiological protection. Over exposure to ionising radiation can cause serious long-term suffering and disability.

Despite their practical importance, the dose-effect relationships, the pathophysiological mechanisms and the influence of the degree to which different tissues are involved are still poorly understood.

This Workshop and Proceedings bring together those at the forefront of research in these areas from all over the world. They review the present state of knowledge and attempt to identify specific problem areas which may lead to recommendations for the improvement of radiological protection and for the better management of radiation accidents.

Radiation Damage to Skin is, therefore, a vital reference work for everyone working in radiation protection and dosimetry.

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Price £18.00 including postage and packing
About 200 pp.; illustrated

Orders to: The Publications Department, The British Institute of Radiology, 36 Portland Place, London W1N 3DG. Tel: 01-580 4085.

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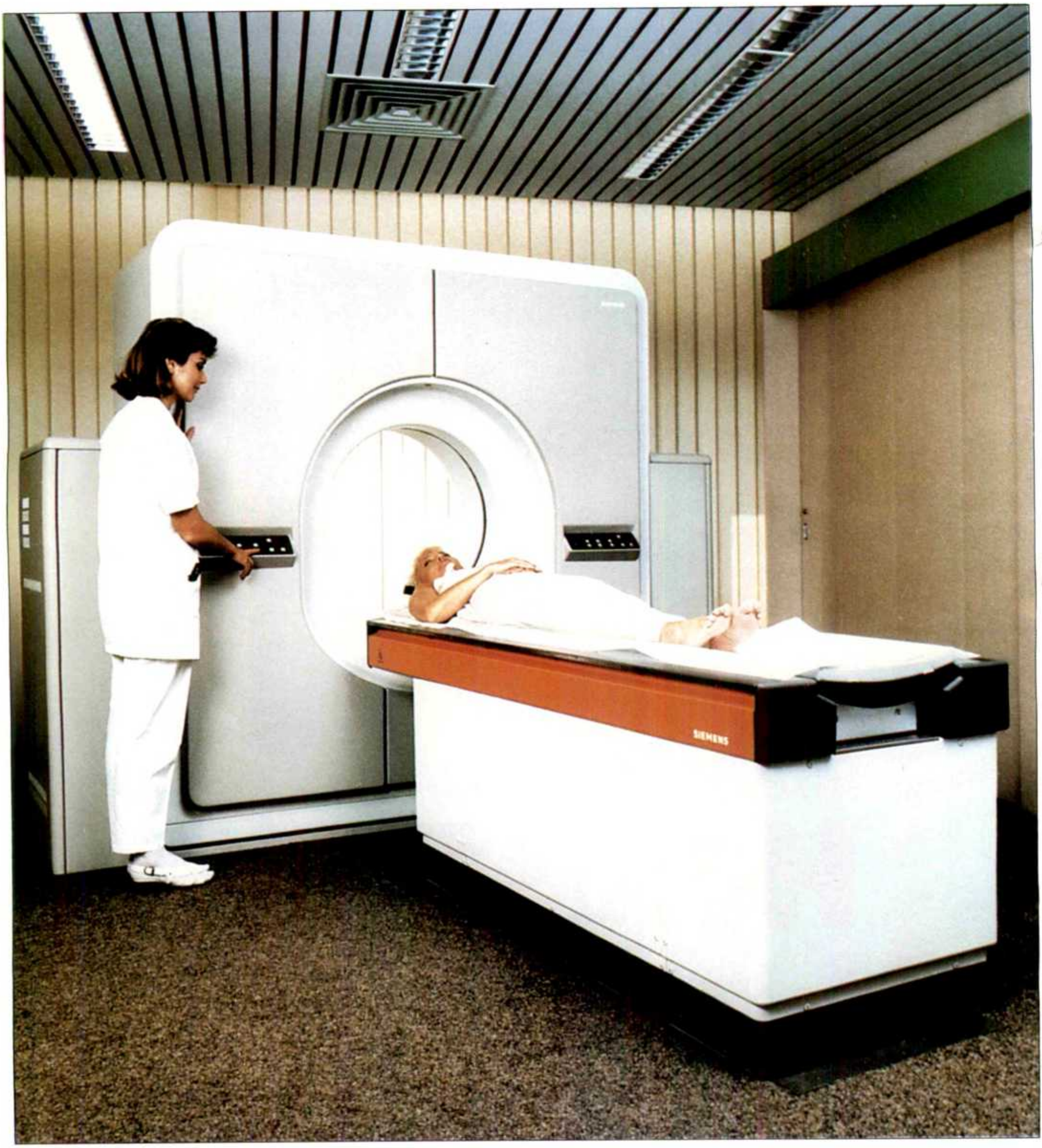

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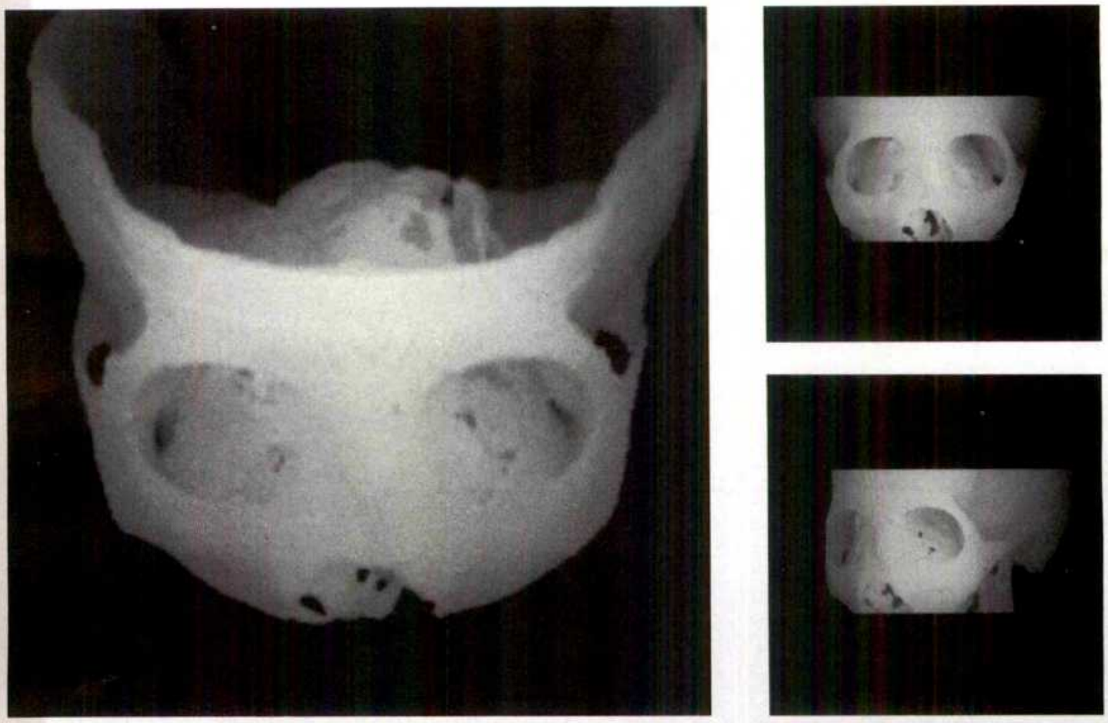

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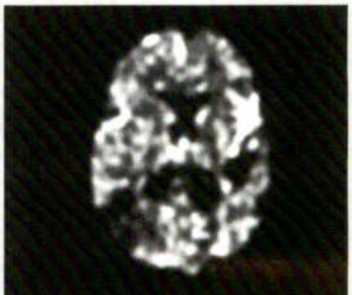

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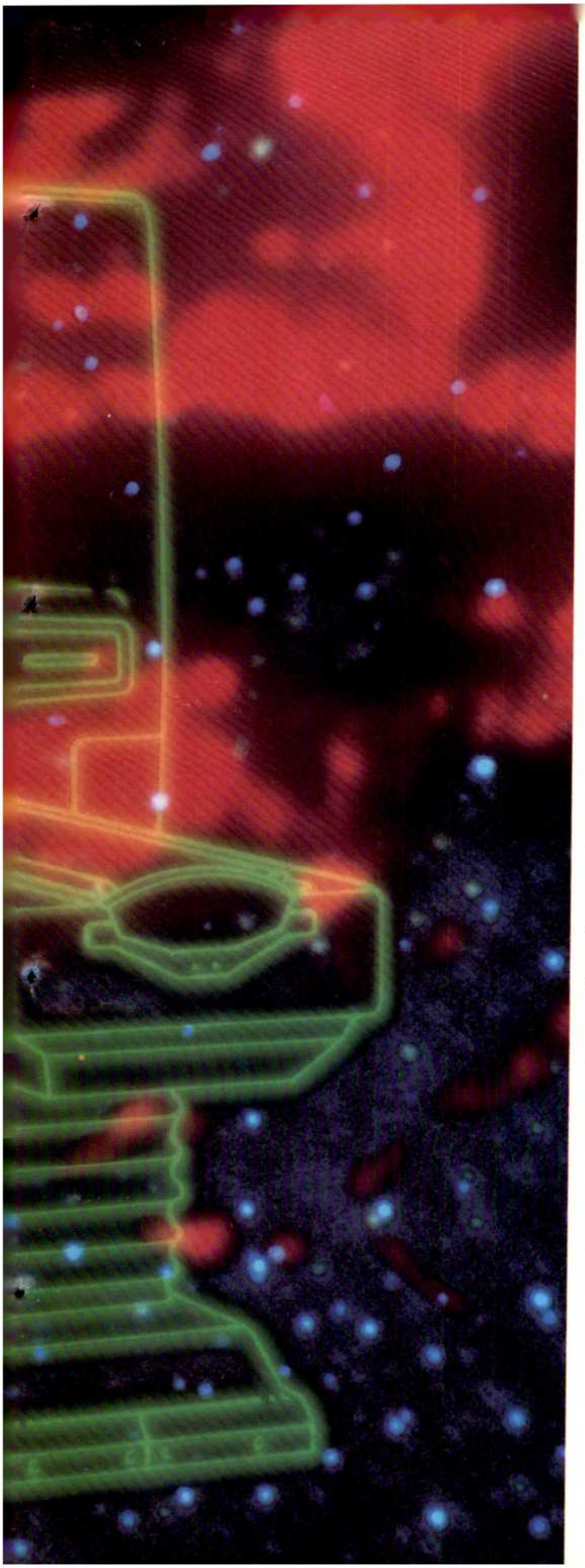

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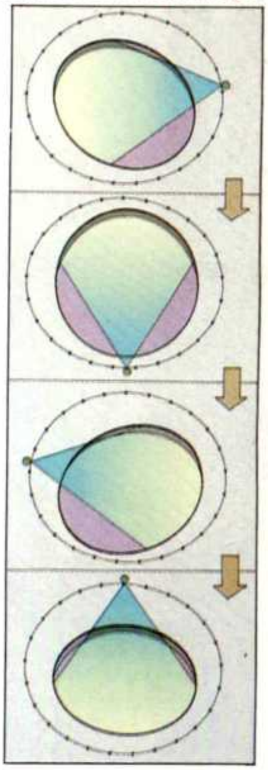

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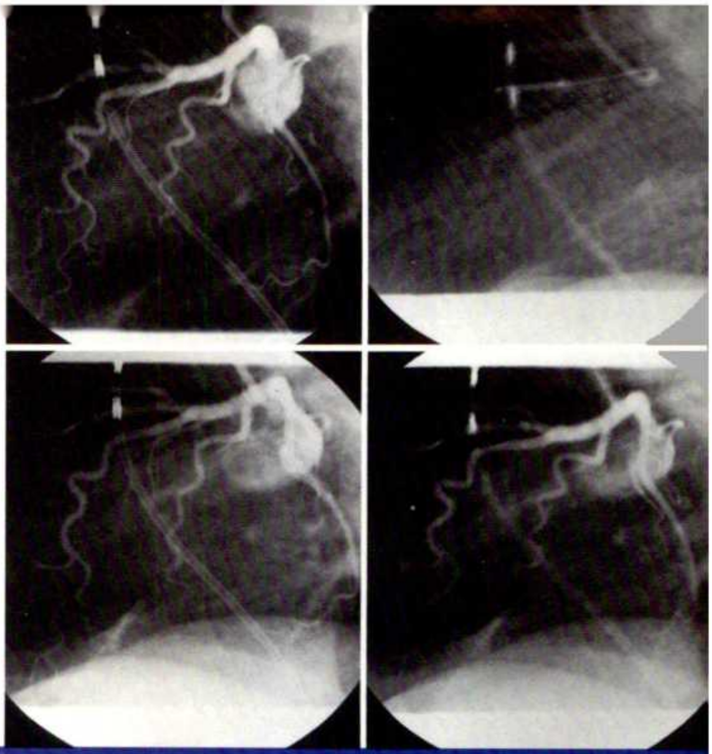

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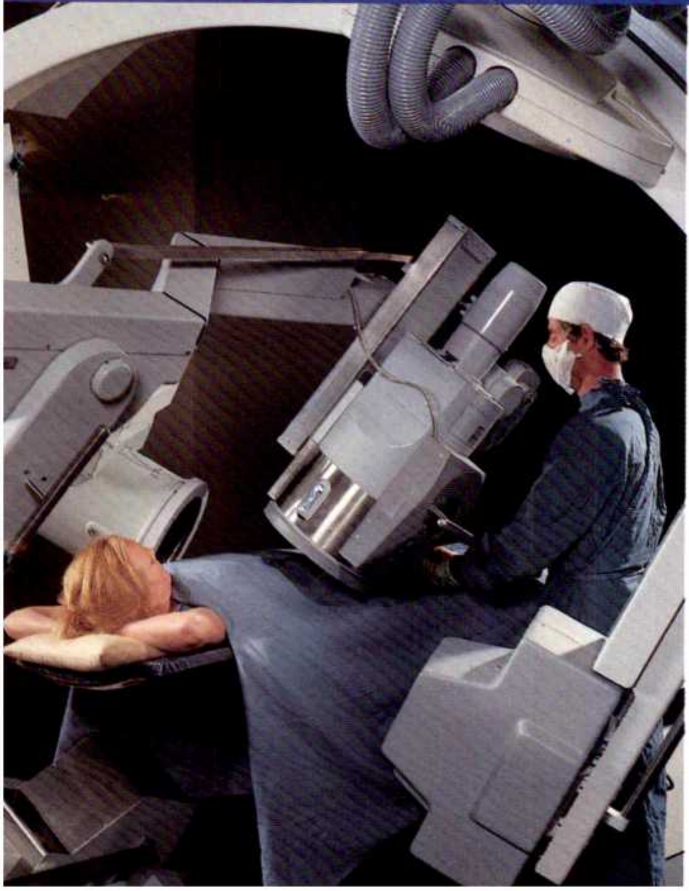

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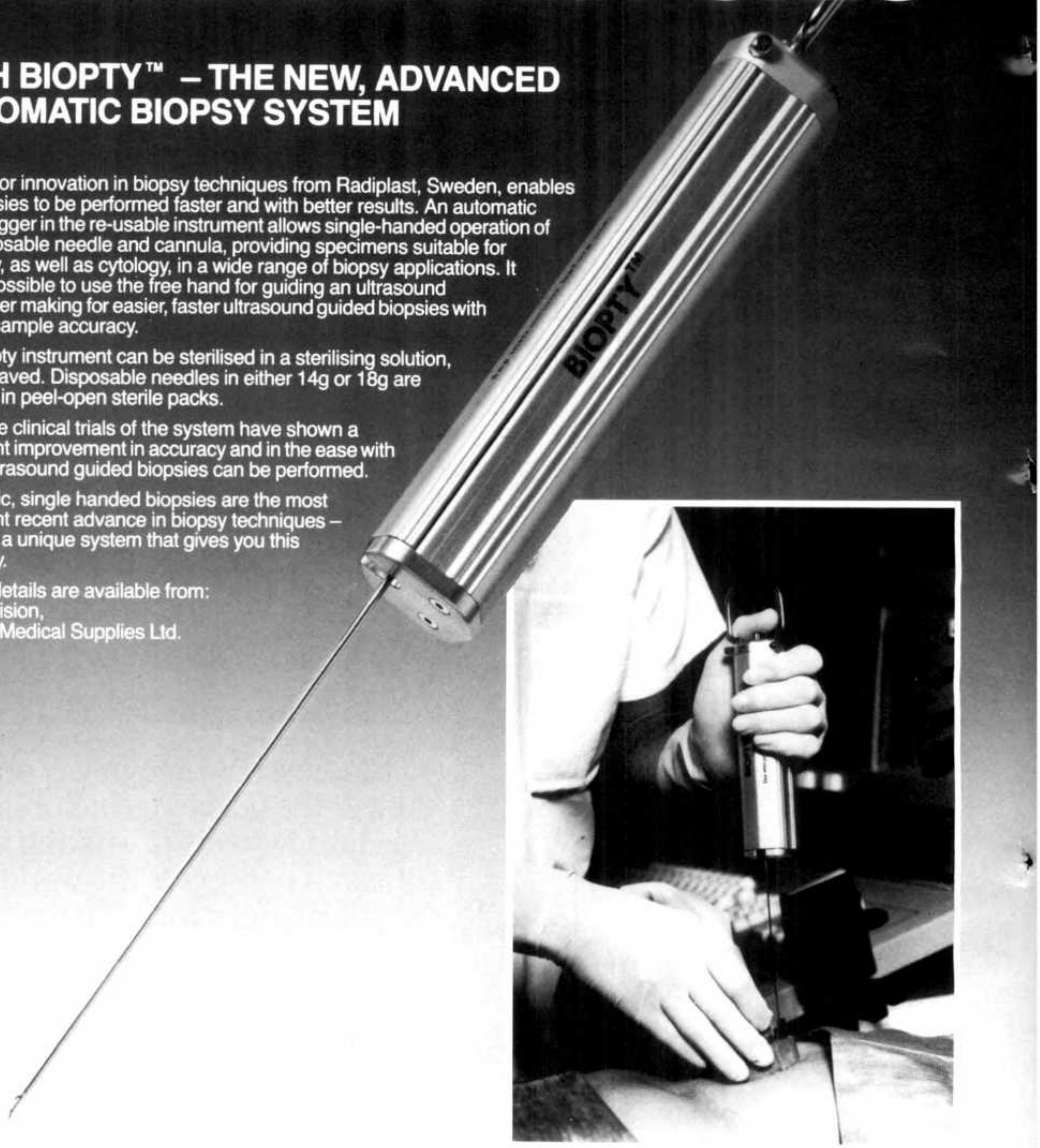

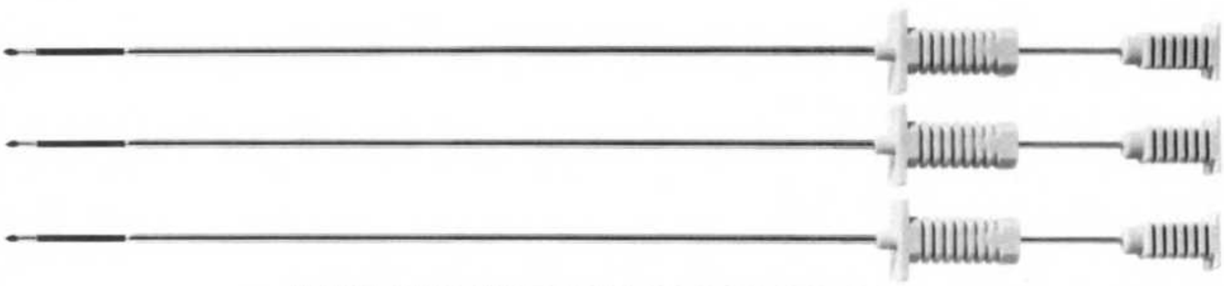

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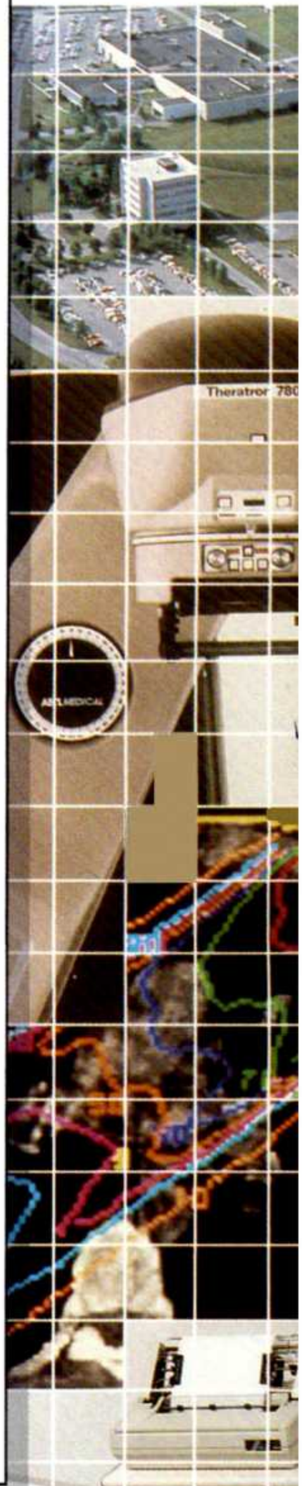

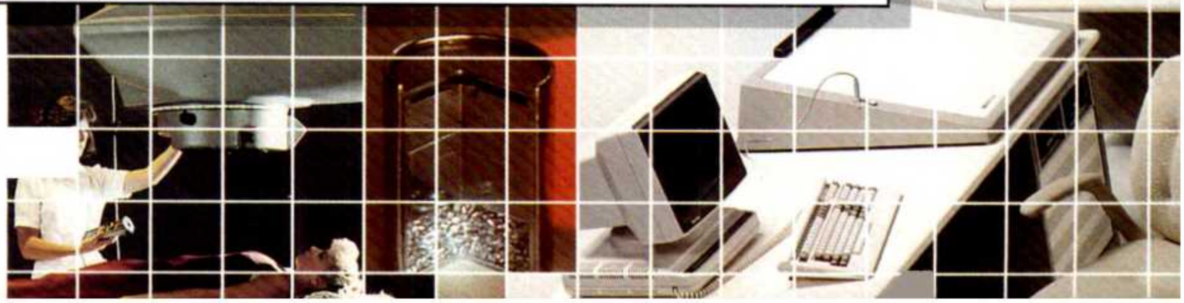

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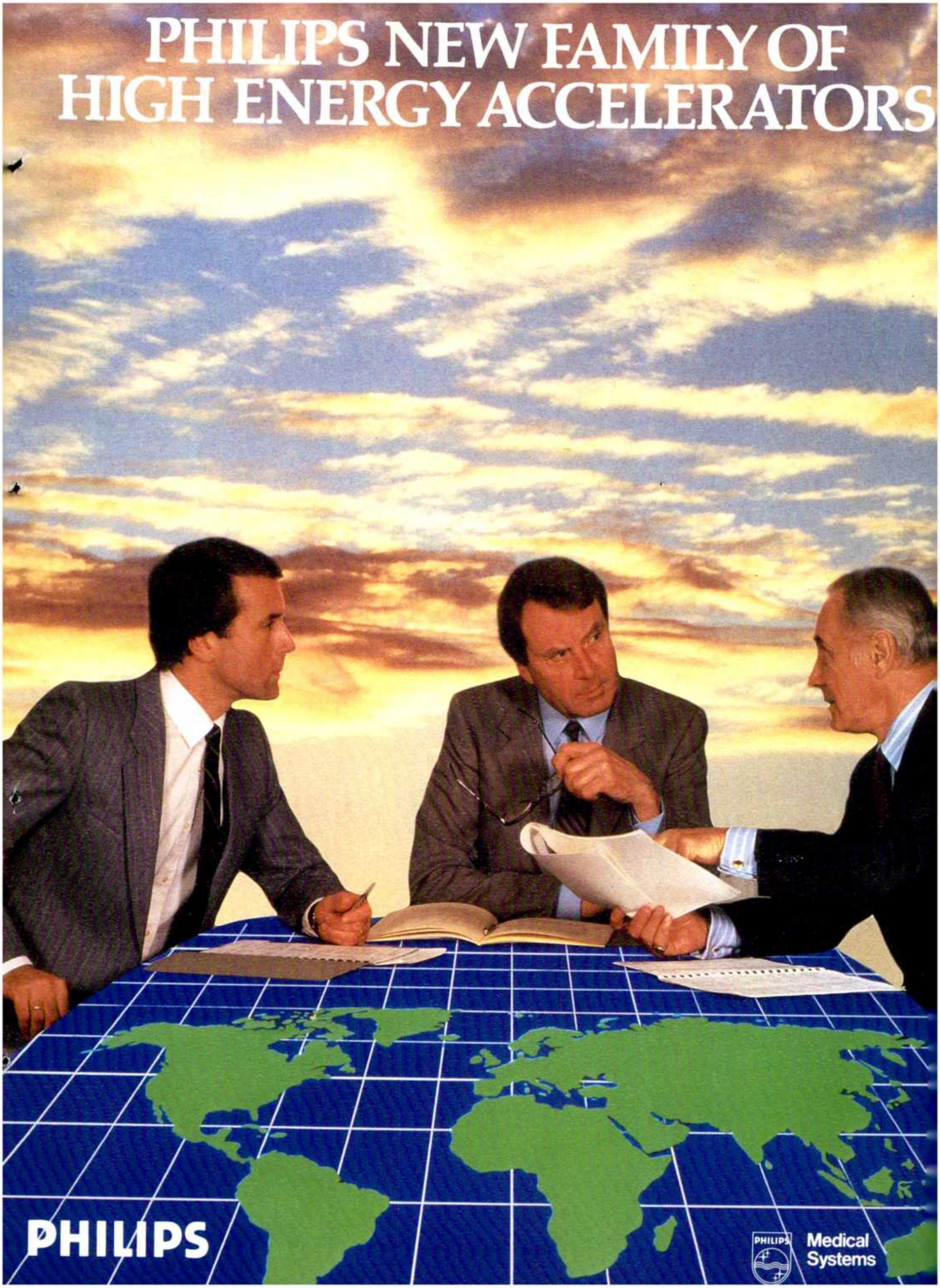
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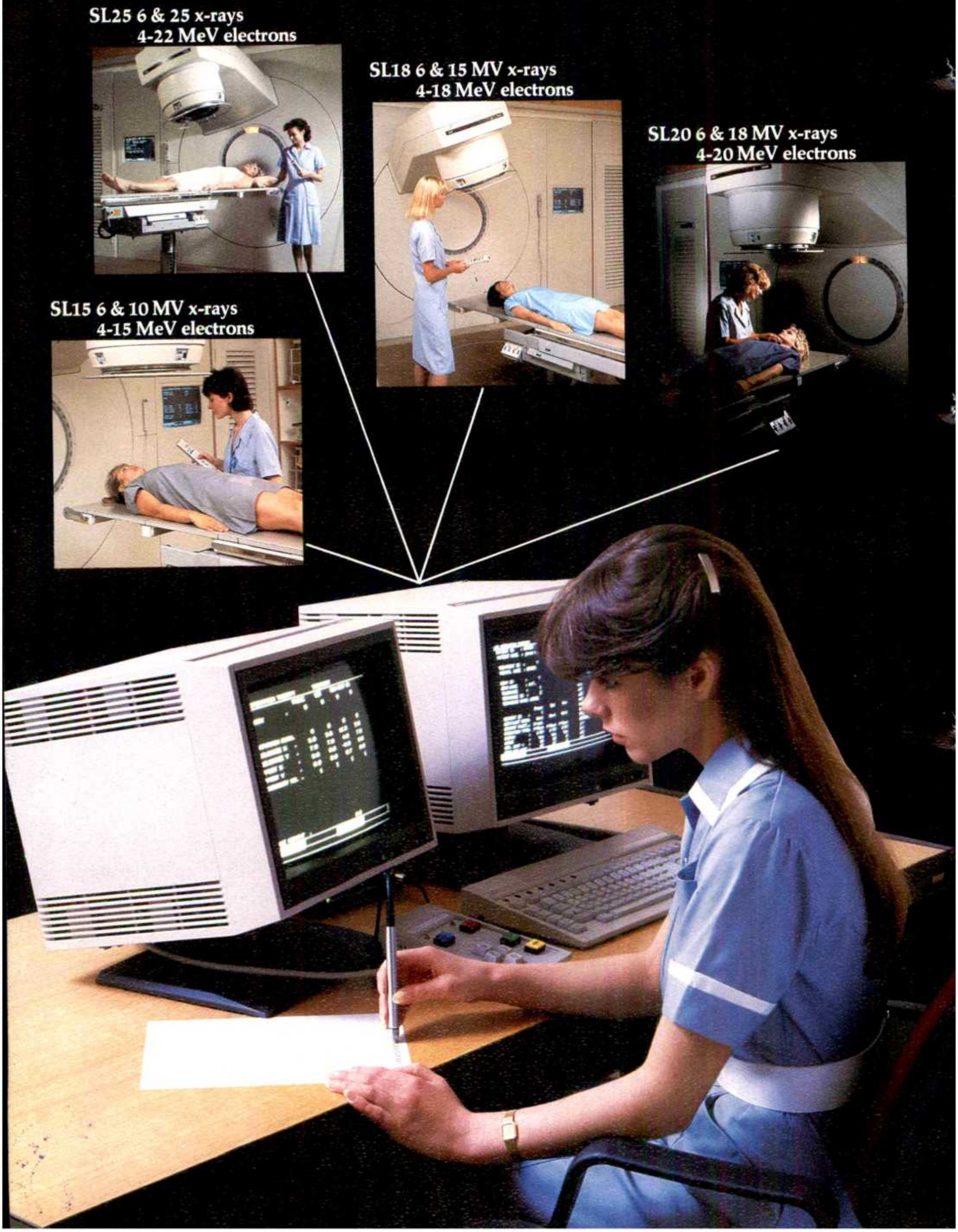

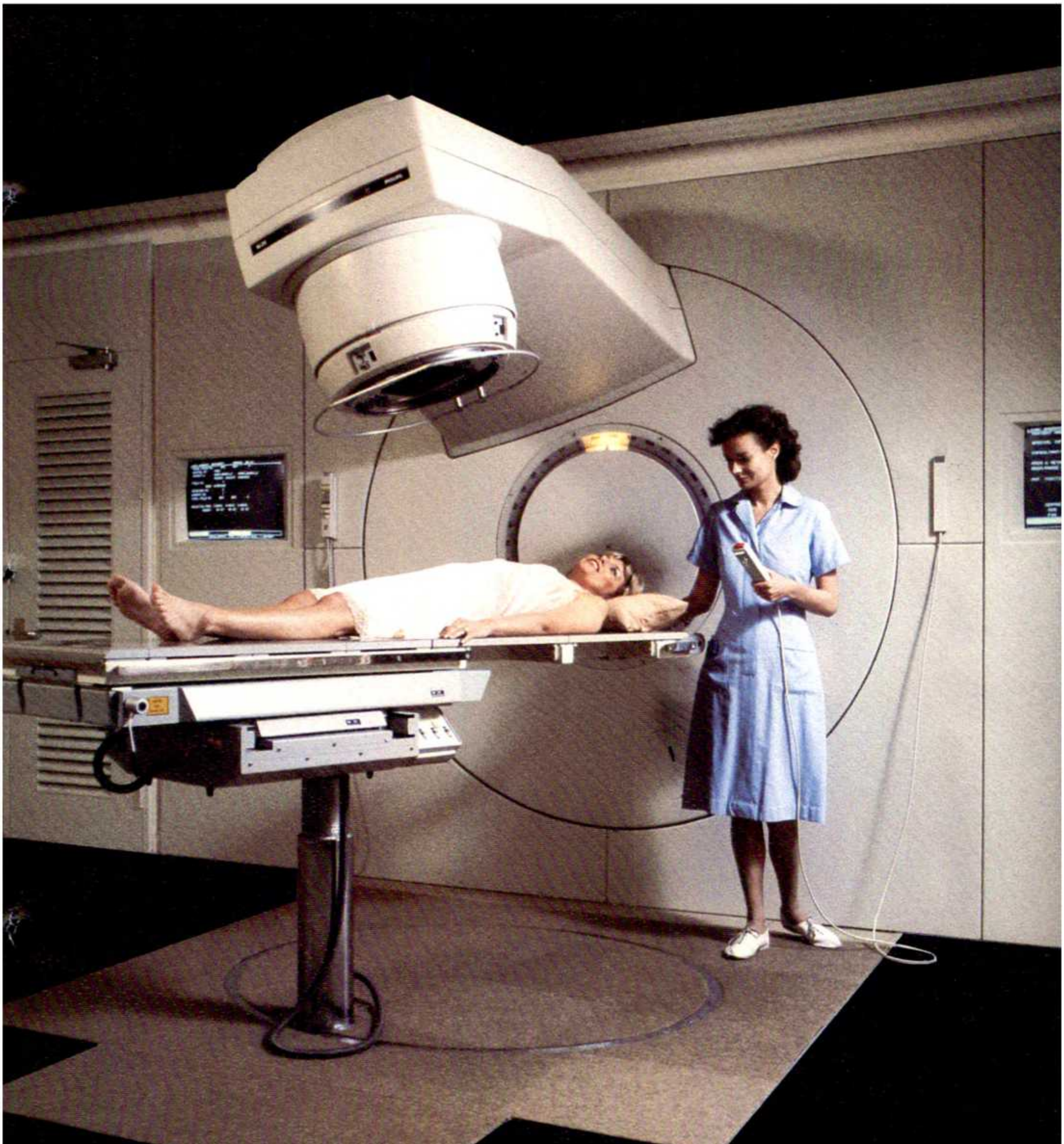

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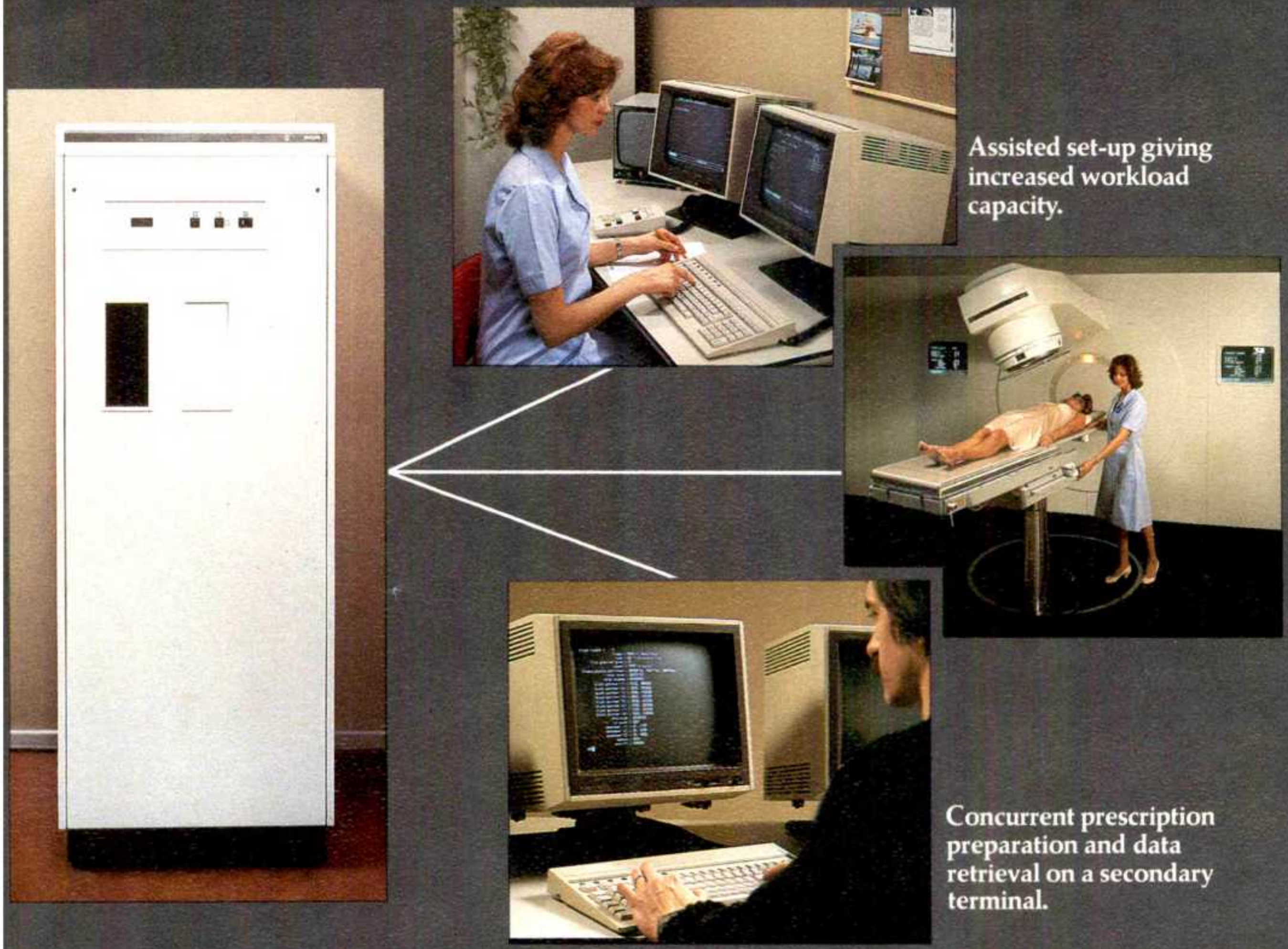

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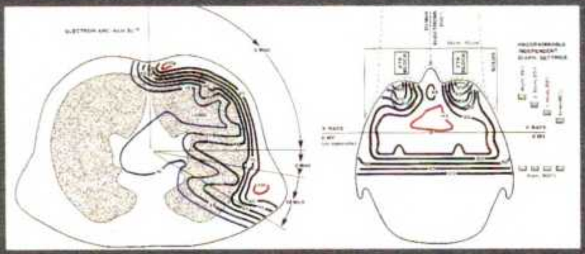

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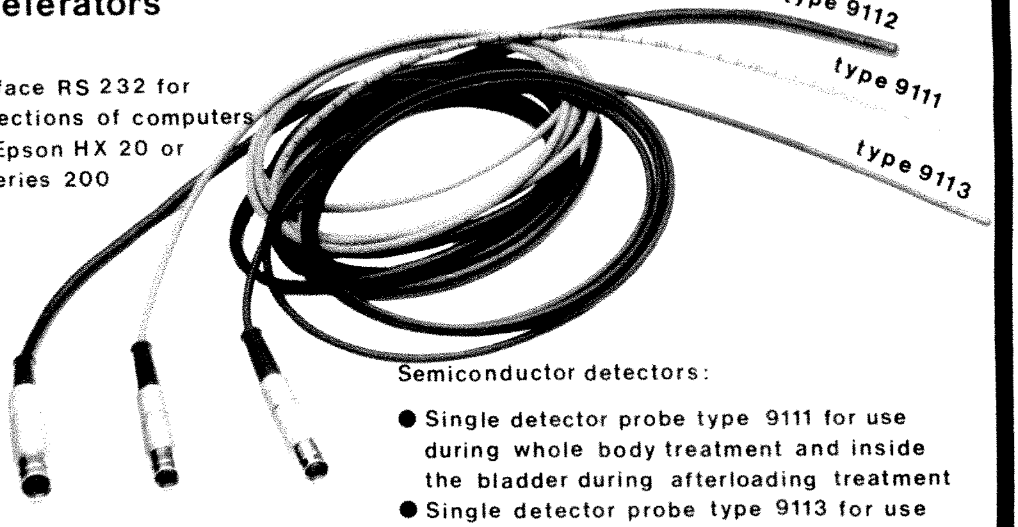

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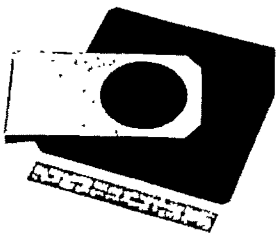

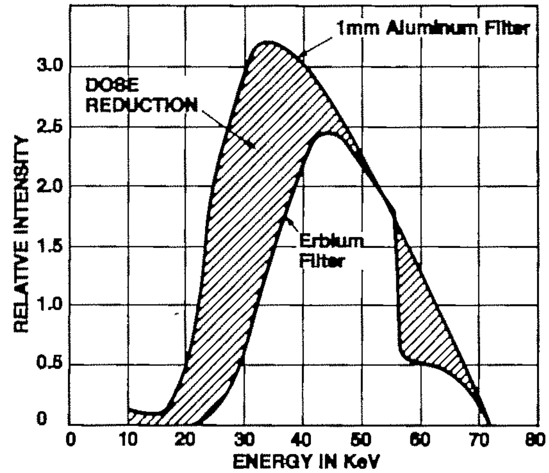

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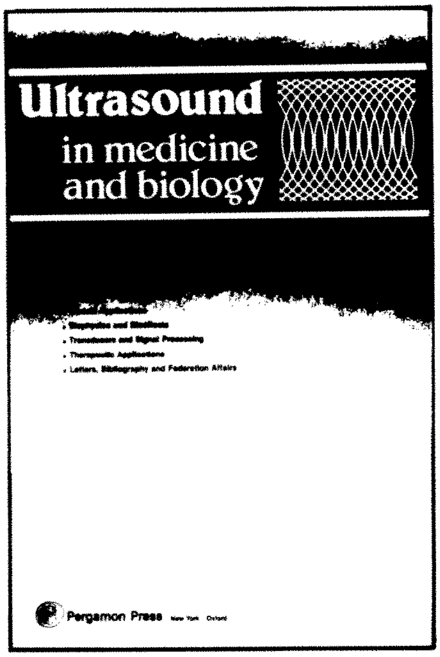

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The British Journal of Radiology

Contrast-enhanced magnetic resonance imaging of tumours of the central nervous system: a clinical review

By M. Graif, M.D. and R. E. Steiner, F.R.C.R.

Department of Diagnostic Radiology, Royal Postgraduate Medical School, Hammersmith Hospital, Du Cane Road, London W12 0HS

(*Received July 1985 and in revised form December 1985*)

ABSTRACT

The clinical application of the intravascular paramagnetic contrast agent gadolinium-DTPA for magnetic resonance imaging (MRI) imaging of tumours of the central nervous system (CNS) has been assessed over the past 3 years. Various patterns of contrast enhancement were observed, and situations in MRI where the administration of contrast medium may be useful have been defined. These include lesions which are isointense with normal brain matter, the separation of tumour from surrounding oedema, evaluation of the degree of blood–brain barrier breakdown, delineation of tumours obscured by overlying calcification on computed tomography (CT) and in the investigation of lesions in anatomical areas where CT has known limitations (brain stem, cervical spine). Changes in relaxation times in normal and abnormal tissues following contrast medium, toxicity and dosage of gadolinium-DTPA, and MRI pulse sequence techniques are reviewed.

Damadian first demonstrated that tumour proton relaxation times were frequently increased when compared with those of host tissues using magnetic resonance spectroscopy (Damadian, 1971; Damadian et al, 1973). These studies were extended by other groups who demonstrated that tumour proton density and relaxation times (T_1 and T_2) were both increased in many neoplastic tissues (Hollis et al, 1973; Hazelwood et al, 1974; Inch et al, 1974; Sarayan et al, 1974). These phenomena (particularly the increase in T_1 and T_2) are the basis for much of the soft-tissue contrast and sensitivity of magnetic resonance imaging (MRI) in tumour detection.

However, increased relaxation times are also produced by other pathological processes (including oedema), leading to difficulties in radiological interpretation. In this situation the ability to produce a selective alteration in relaxation time of a target tissue may be useful.

Paramagnetic materials can be used to produce such changes *in vivo* (Brasch et al, 1983) and, after several years of animal work, one such agent, gadolinium-diethylene triamine penta-acetic acid (Gd-DTPA) is now being used in clinical practice.

In this paper the basic principles of the action of paramagnetic contrast agents are reviewed. The role of MRI pulse sequences in demonstrating Gd-DTPA enhancement and indications for its clinical use in tumour diagnosis are discussed.

BASIC PRINCIPLES

General approach

The main parameters determining soft-tissue contrast involved in MRI are proton density, spin-lattice relaxation time (T_1) and spin-spin relaxation time (T_2). These last two time constants describe the exponential return to equilibrium of proton magnetisation after excitation (Gadian, 1982; Pykett et al, 1982).

Pulse sequences with varying dependence on T_1 and T_2 are used in MRI since they selectively alter the contrast between soft-tissue components (Taylor & Bore, 1981; Pykett et al, 1982; Partain et al, 1983; Rosen & Brady, 1983).

A different approach to achieving satisfactory soft-tissue contrast is the use of paramagnetic ions to change tissue T_1 and T_2, but an important corollary to this is the fact that it is necessary to choose pulse sequences with the appropriate dependence on T_1 and T_2 to detect these changes.

Paramagnetic agents

Paramagnetic substances possess a permanent magnetic moment due to the presence of an unpaired spin (proton, neutron and electron). When such a substance is introduced into a biological microenvironment it acts as a relaxation centre. The local magnetic field produced by this substance shortens the T_1 and T_2 relaxation times of the surrounding hydrogen nuclei (Bloembergen et al, 1948; Young et al, 1981b; Mendonca-Dias et al, 1983; Gadian et al, 1985).

The degree of T_1 shortening depends upon several factors, including the effective magnetic moment of the ion, the concentration and average distance between the paramagnetic ions and the resonating nucleus (Bloembergen et al, 1948; Runge et al, 1983; Gadian et al, 1985).

Paramagnetic ions have been used since 1946 to alter relaxation times of nuclei (Bloch et al, 1946). The paramagnetic ions include Mn^{2+}, Cu^{2+}, V^{2+}, Fe^{3+}, Gd^{3+} and Cn^{3+}. In addition to metal ions, other paramagnetic substances such as nitroxide stable free radicals and molecular oxygen may be used. Manganese, iron and gadolinium are very effective agents but toxic in their free form. Experimental and clinical studies demonstrate that gadolinium, when chelated to DTPA, forms the least soluble and safest compound with effective paramagnetic moment studied so far (Pople et al, 1959; Runge et al, 1983; Brasch et al, 1984).

Gadolinium-DTPA

The gadolinium ion (Gd^{3+}) has seven unpaired electrons in the 4-f electron orbitals, which provide the strong paramagnetic properties (Pople et al, 1959). Chelation with diethylene triamine penta-acetic acid (DTPA) reduces the proton relaxation effects as it occupies eight of the coordination sites, leaving only one or two sites open for fast-changing with water protons. Chelation with DTPA is necessary since Gd^{3+} in its free ionic form is toxic to the liver, spleen and bone marrow (Weinmann et al, 1984). The chelated compound (Gd-DTPA) has a high molecular stability and an intravenous tolerance similar to that of diatrizoate. The neural tolerance of Gd-DTPA is several times better than that of diatrizoate. Furthermore, Gd-DTPA is a poor activator of the complement system and is not expected to produce anaphylactoid reactions (Weinmann et al, 1984). This stable compound is rapidly excreted unchanged via glomerular filtration (85% within 3 h). The distribution of intravenously injected Gd-DTPA is primarily in the intravascular, extracellular space and it rapidly passes into the extravascular, interstitial space. Gd-DTPA has a high molecular weight (590 approx.) which is similar to that of diatrizoate, which probably accounts for the fact that it does not cross the normal blood–brain barrier. Animal and clinical studies have shown focal contrast enhancement paralleling that seen on CT, suggesting the passage of Gd-DTPA through the damaged blood–brain barrier (Brasch et al, 1984; Carr et al, 1984a, b; Graif et al, 1985).

Magnetic resonance imaging considerations

Changes in the concentration of Gd-DTPA, as well as selective use of different pulse sequence techniques, is known to determine the signal intensity on MRI in different types of pathology.

Theoretical studies have demonstrated that increasing concentrations of Gd-DTPA produce a progressive shortening of T_1 and T_2 relaxation rates (Weinmann et al, 1984; Gadian et al, 1985) but not necessarily a linear increase in signal intensity. It was demonstrated *in vitro* and *in vivo* using different spin sequences that, for low concentrations of Gd-DTPA (below 1 mmol per kg of body weight), the shortening of T_1 gives an increase in signal intensity which is eventually negated by the reduction in T_2 at higher concentrations (Gadian et al, 1985). There is an optimum concentration beyond which the shortening of T_2 dominates signal intensity and the enhancement is reduced or even reversed (Taylor & Bore, 1981; Weinmann et al, 1984; Carr et al, 1984c, Curati et al, 1986; Gadian et al, 1985). Even when using concentrations of Gd-DTPA of 0.1 mmol per kg of body weight, the selective application of various pulse sequences has a significant impact on the level of enhancement, as shown by sequence comparison studies. T_1 weighted sequences, such as inversion recovery (IR) and short TR, short TE spin-echo (SE) may exploit positively the decrease in T_1, showing a major increase in signal intensity. On the other hand, T_2 weighted sequences (*e.g.* longer TR, longer TE, SE) will reflect the negative influence of T_2 shortening, displaying a minor increase in signal intensity or even a negative enhancement (Schonner et al, 1984; Weinmann et al, 1984; Bydder et al, 1985a; Graif et al, 1985).

TABLE I

CLINICAL DIAGNOSES

Malignant brain tumours	
Primary: low degree of malignancy	8
high degree of malignancy	7
Suspected primary tumours (no histology)	2
Secondary	7
Acoustic neuromas	12
Meningiomas	6
Tumours involving spinal cord	5
Total no. of patients	47

CLINICAL STUDIES

Forty-seven patients with tumours of the central nervous system (CNS) are reviewed (Table I). In 26 there was histological confirmation of the tumour. In the remainder of the patients the diagnosis was made on clinical and radiological criteria.

Magnetic resonance imaging was performed with a superconducting magnet operating at 0.15 T. The sequences used are listed in Table II. The contrast agent Gd-DTPA was injected intravenously at a dose of 0.1 mmol/kg, after a pre-contrast baseline scan had been obtained. All sequences were repeated after injection of contrast medium. Calculated T_1 and T_2 maps were obtained using the method previously described (Young et al, 1982). Biochemical tests, including levels of blood urea, creatinine, electrolytes

TABLE II

LIST OF PULSE SEQUENCES EMPLOYED FOR THE STUDY

Pulse sequence	TR (ms)	TI (ms)	TE (ms)
IR	1500	500	44
SE	544		44
SE	1500		44
SE	1500		80

TR = repetition time, TI = inversion time, TE = echo time, IR = inversion recovery, SE = spin echo.

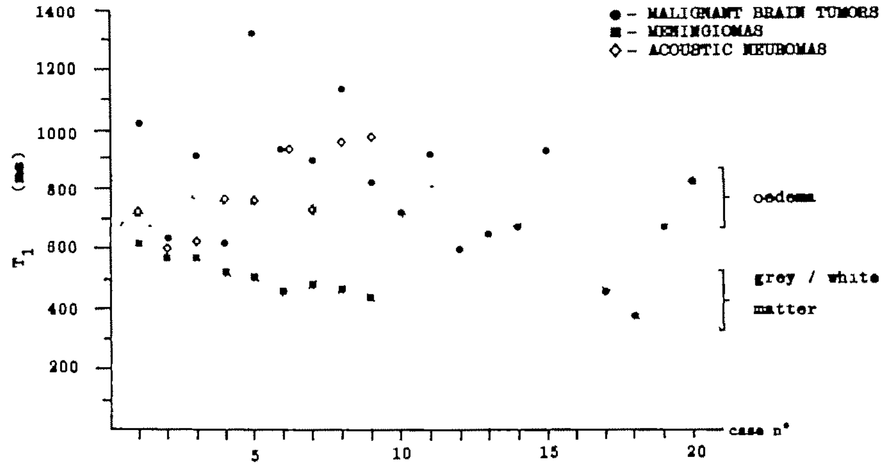


Fig. 1

Distribution of T_1 values (vertical axis) of different malignant and benign tumours (horizontal axis) in relation to the T_1 range of oedema and normal brain matter.

(Na^+, K^+, HCO_3^-), liver function tests, serum iron and a blood screen (haemoglobin, red blood cell count, platelets), were performed before and twice (2 h and 24 h) after contrast medium injection in each patient.

Normal brain

White matter displayed a non-significant reduction in T_1 (1%) and a slight reduction in T_2 (10%) after contrast medium administration. The corresponding T_1 and T_2 decreases in grey matter were 8% and 13–14%, respectively. These results were obtained by systematic pre- and post-contrast medium relaxation-time measurements in 26 patients. Similar results were reported by Felix et al (1984) in a series of 34 patients.

Oedema

The mean T_1 value of oedema as measured on the pre-contrast medium images in 16 cases was 760 ± 80 ms (Fig. 1). In only six of these cases was it possible to obtain a satisfactory separation of tumour from surrounding oedema. Relaxation times of oedema did not change after contrast injection (Brasch et al, 1984; Graif et al, 1985). Exceptions were encountered in five cases in our experience where portions of the peritumoral areas considered as oedema displayed a clear reduction in T_1 (22–33%), while the remaining portions were unchanged.

Malignant brain tumours

Post-contrast medium increase in pixel value was observed in 22 out of 24 tumours studied by MRI. The patterns of enhancement were diffuse, patchy, ring-shaped and linear. Systematic analysis of 17 cases revealed a mean post-contrast medium reduction of 22% in T_1 and 21% in T_2. Maximal enhancement was noted 20–40 min post-injection. This persisted up to 210 min in one case which was followed for that length of time. Comparison of the degree of enhancement in three groups of different malignancy revealed a mean T_1 decrease of 16% in primary tumours of low grade of malignancy, a 29% T_1 decrease in primary tumours of high grade of malignancy and a mean T_1 decrease of 33% in metastases (Graif et al, 1985). This reduction of T_1 was expressed as increase in signal intensity.

Acoustic neuromas

Marked increase in signal intensity was observed in all 12 tumours investigated. This was due to a mean reduction of 50% in T_1. This enabled the demonstration of one very small intracanalicular tumour which was missed by air computed tomography (CT) technique. It also enabled differentiation of recurrence of a tumour from post-operative changes (Curati et al, 1986).

Meningiomas

All six meningiomas studied with Gd-DTPA displayed post-contrast medium enhancement. This was due to a reduction in T_1 of 10–41%. The most efficient sequence was IR as it was sensitive to both pathological change and contrast enhancement (Bydder et al, 1985a). The T_2 weighted SE was sensitive to the pathology, but of little use in demonstrating enhancement.

Toxicity

No significant changes in the biochemical or haematological tests were observed except for a transient rise in the serum iron in two patients 2 h after injection. The serum iron levels returned to normal in both patients within 24 h

Clinical Considerations

Analysis of contrast medium-enhanced MRI studies in 47 patients has been carried out and the clinical literature on MRI in CNS tumours is reviewed. Several radiological situations have emerged where Gd-DTPA may play a particular diagnostic role.

Isointensity of a lesion with normal brain tissue

A survey of 279 brain tumours revealed no increase in T_1 and T_2 values, with respect to normal brain, in 12% of the cases (MacKay et al, 1985). This tumour

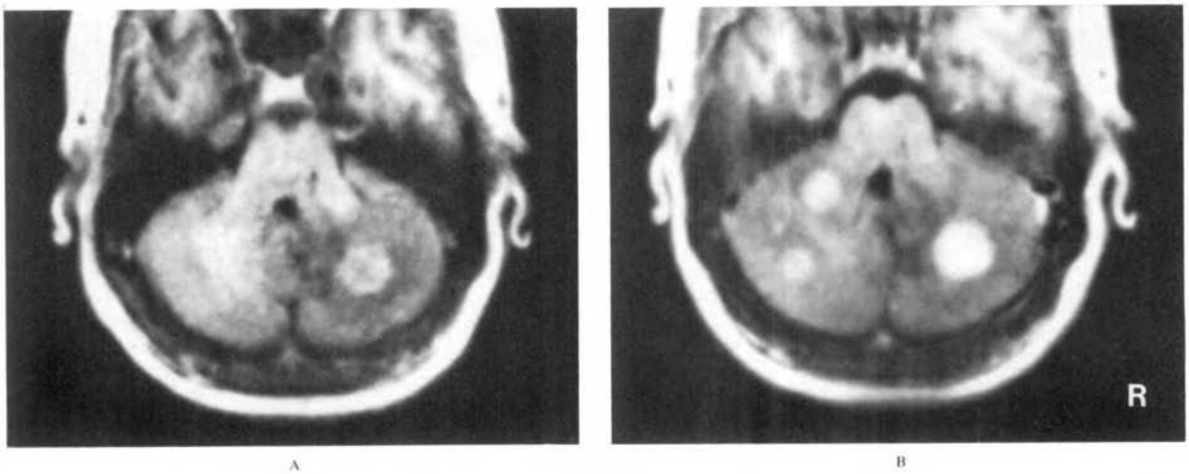


FIG. 2.

Secondary lesions of malignant melanoma in the posterior fossa: $IR_{1500/500}$. Only one lesion is clearly visible before contrast (A). Two additional lesions become evident after contrast injection (B).

study and those reported by other authors included malignant melanomas, tumours containing blood and fat, meningiomas, acoustic neuromas, pituitary adenomas and Grade I astrocytomas following radiotherapy (Mills et al, 1984; Zimmerman et al, 1985). In our series, the extra-axial tumours (four out of nine meningiomas and one acoustic neuroma) more frequently displayed T_1 and T_2 values within the range of those of normal brain tissue, although similar values were observed also in two malignant brain neoplasms (Figs 1, 2). In two cases (metastatic melanoma and penetrating olfactory neuroblastoma) the lesions were not seen on the initial scan, but were displayed after contrast medium administration. Administration of Gd-DTPA provided a marked T_1 and T_2 reduction (10–50%) in both intra- and extra-axial lesions, enabling a clear demarcation from the surrounding tissues which did not change after contrast medium

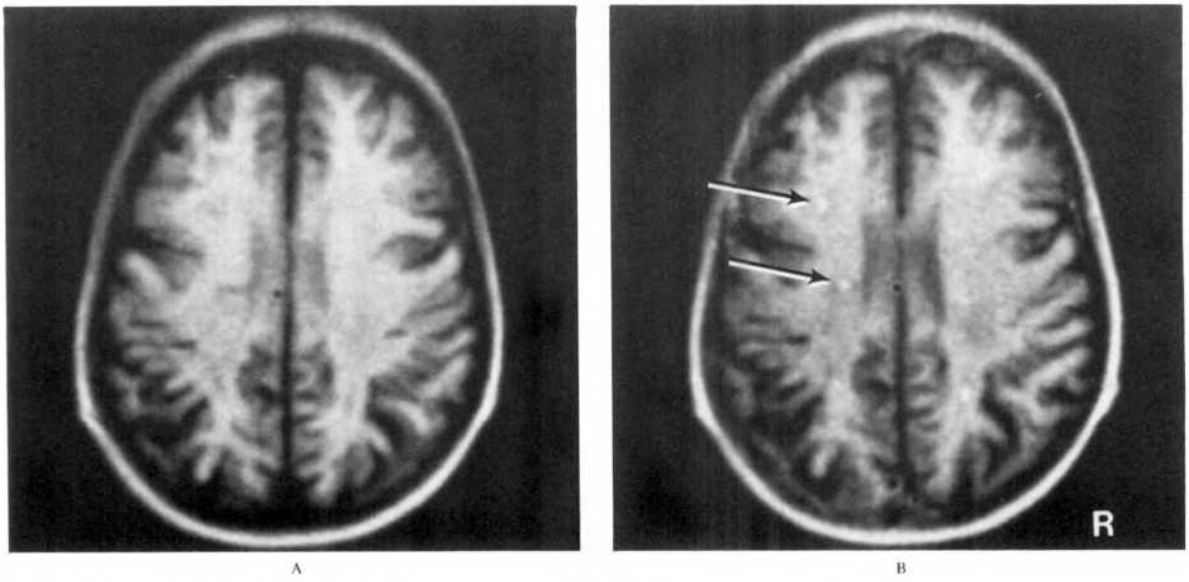


FIG. 3.

Metastatic spread from breast carcinoma. No lesion is observed on the $IR_{1500/500}$ image (A). After enhancement with contrast medium (B) several small lesions become evident (arrows).

administration. Rich vascularisation in the extra-axial tumours and blood–brain barrier breakdown in the intra-axial lesion probably account for the enhancement effects.

Isointensity due to partial-volume averaging

Small lesions (smaller than slice thickness and individual voxel) tend to be obscured and merge with the surrounding tissue because of partial-volume effect (Pullan et al, 1981; Zatz, 1981) in X-ray CT. A similar phenomenon occurs with MRI of small lesions with relaxation times similar to those of normal brain. Magnetic resonance imaging with Gd-DTPA enhancement reduces T_1 relaxation times, allowing small lesions to become conspicuous by an increase in their signal intensity.

In our experience this phenomenon occurred in three cases of small metastatic lesions from primary tumours in the lung, breast and ovary. All these lesions became apparent only after the injection of contrast agent (Fig. 3).

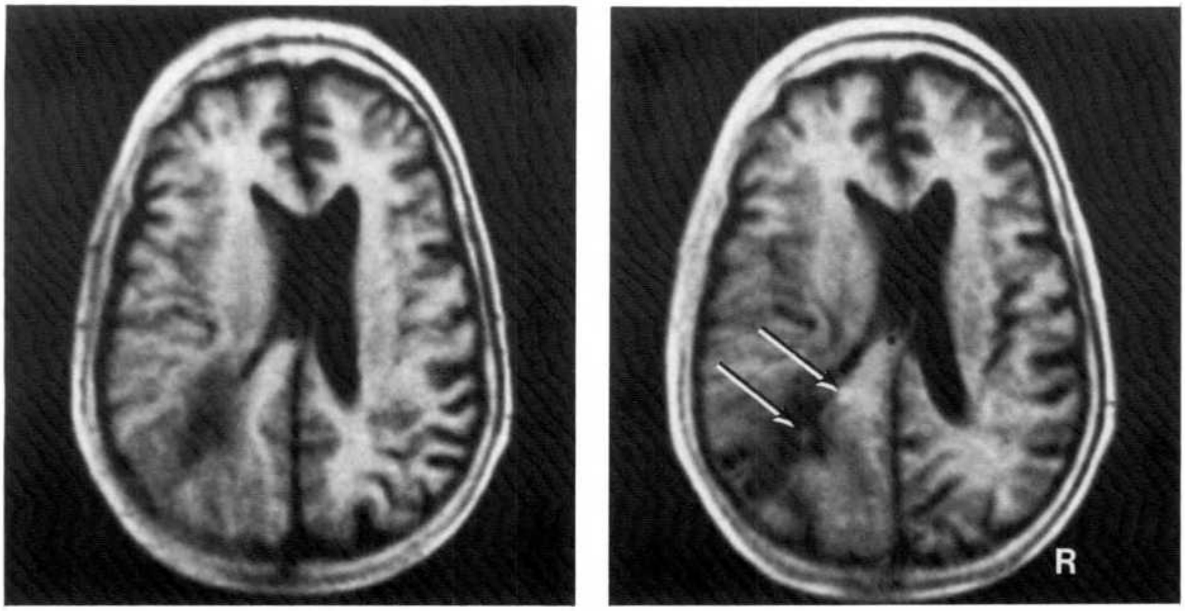
Isointensity of tumours with surrounding oedema

Several workers have reported diagnostic difficulties in separating tumour margins from oedema (Bydder et al, 1982; Brant-Zawadzki et al, 1984; Bydder et al, 1984; Graif et al, 1985) using both IR and SE techniques. In the series studied here, both tumour and oedema displayed prolonged T_1 and T_2 which frequently overlapped. Several acoustic neuromas were found to have T_1 and T_2 values in the range of oedema, but were rarely surrounded by it and, therefore, this did not present a diagnostic problem.

A mean decrease of 21% in T_1 and of 26% in T_2 of tumours was observed after the injection of Gd-DTPA, while the peritumoral oedema remained unchanged, probably due to preservation of the integrity of the blood–brain barrier in the region of oedema (Figs 4, 5). These findings are very similar to those obtained in CT scanning. In five of our patients, areas considered as oedema on the pre-contrast scan displayed subsequent enhancement, suggesting breakdown of the blood–brain barrier and, hence, tumour infiltration.

Assessment of the degree of malignancy

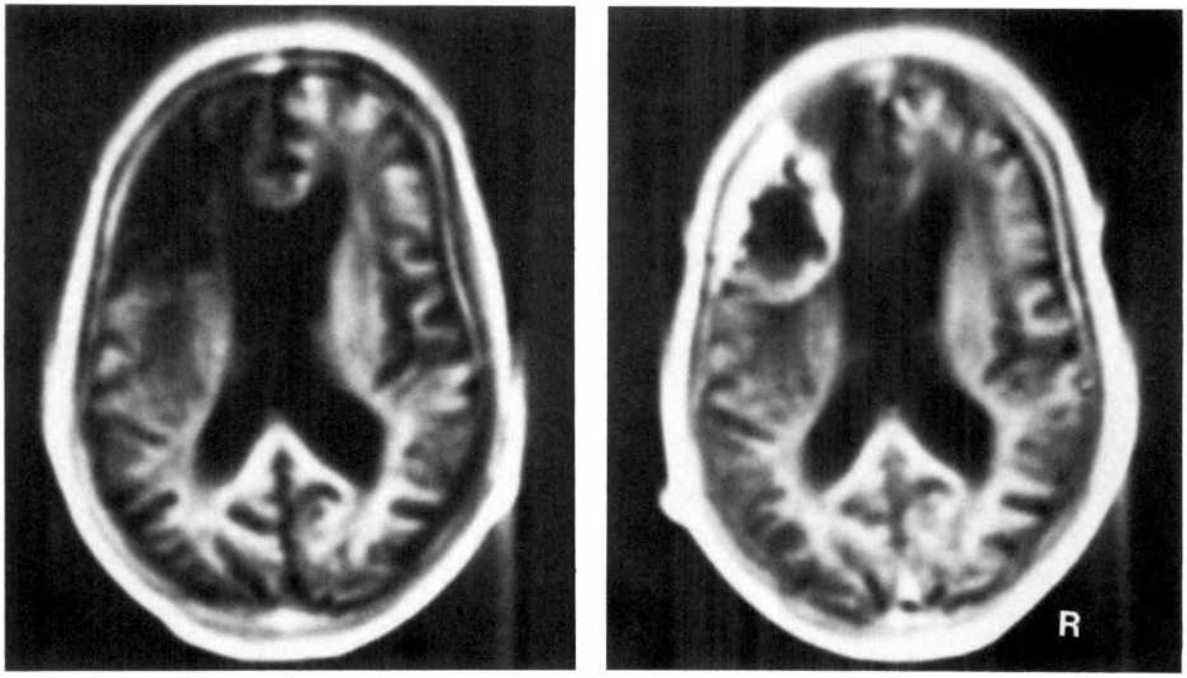
It has been suggested that the degree of contrast enhancement with CT scanning in intra-axial tumours may be of clinical significance in the grading of tumour malignancy by reflecting the degree of blood–brain barrier breakdown. In low-grade gliomas, for example, the newly formed capillaries resemble normal cerebral capillaries. On the other hand, in more malignant tumours, the new capillaries are fenestrated with vesicule formation; the blood–brain barrier is therefore incomplete and allows more enhancement (Caille et al, 1980; Sage, 1982). Analysing 17 malignant tumours, the degree of enhancement in MRI was found to correlate with the grade of malignancy by displaying



A B

FIG. 4.

Metastates from carcinoma of the ovary. The pre-contrast medium $\mathrm{IR}_{1500/500}$ scan (A) shows a region of oedema on the left. After contrast medium enhancement (B) two lesions are depicted (arrows), one of which was isointense with oedema and the other with normal white matter.

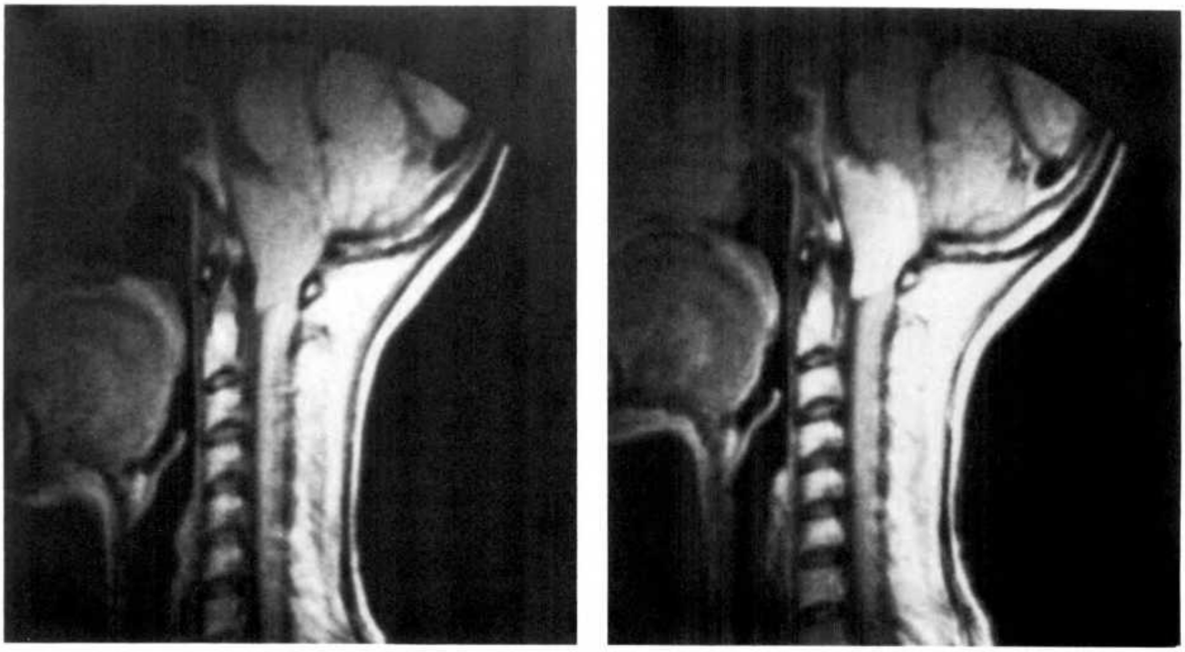


A

B

FIG. 5.

Astrocytoma Grade IV on pre-contrast medium $IR_{1500/500}$ is displayed as an area of oedema in the left frontal region (A). A repeat scan 10 min after contrast medium injection shows ring enhancement of the lesion (B).

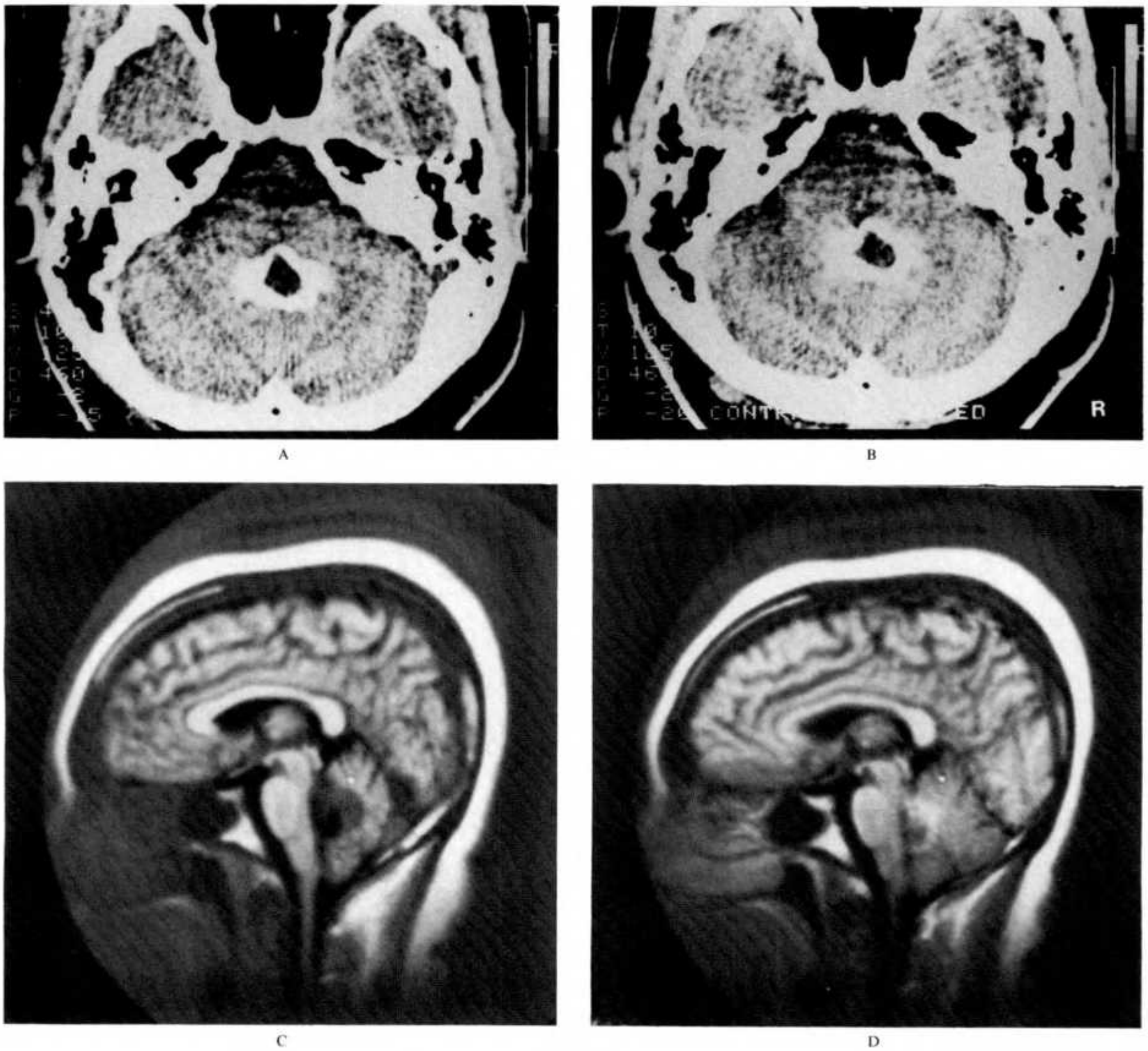


A

B

FIG. 6.

Meningioma at the level of the foramen magnum. $SE_{544/44}$ images before (A) and after (B) enhancement with contrast medium.



A

B

C

D

FIG. 7.

A primitive neuroectodermal tumour adjacent to the fourth ventricle: CT scans before (A) and after (B) contrast enhancement. A calcified ring obscures the assessment of contrast medium enhancement. Inversion recovery MR images in the sagittal plane before (C) and after (D) contrast enhancement show the full extent of the lesion.

a T_1 decrease of 16%, 25% and 33% in low-grade, high-grade and metastatic malignancies, respectively (Graif et al, 1985).

Other indications

In three areas, brain stem, cervical spine and, to some extent, posterior fossa, MRI is known to have a considerable advantage over other imaging modalities. This is mainly due to the absence of bone artefacts common on CT and the ability to image in the sagittal and coronal planes without recourse to image reconstruction (Young et al, 1981a; Randell et al, 1983; Modic et al, 1984; Norman et al, 1984; Lee et al, 1985). Often, MRI is the only method capable of demonstrating the pathological process (Fig. 6). To obtain maximum information the use of paramagnetic intravenous contrast medium should be considered.

Lesions may be obscured by hyperdensities on CT: extensive calcification may obscure enhancement on CT. Calcification gives a low MRI signal due to a reduced mobile proton content. The effect of contrast enhancement on MRI of a heavily calcified lesion can be evaluated without difficulty (Fig. 7).

In this subgroup of patients the indications for contrast medium enhancement are the same as those discussed for patients with brain tumours. These include visualisation of isointense tumours, differentiation of tumour from oedema and assessment of vascularity and blood–brain barrier integrity.

In a recent publication Bydder et al (1985b) discuss the results of contrast medium enhancement with Gd-DTPA in 10 patients with cervical intraspinal tumours. All tumours enhanced with contrast medium and there was a clear separation of extra- from intramedullary lesions. It appears from this study that the use of contrast agents in spinal cord tumours parallels its use in the brain.

CONCLUSION

Gd-DTPA has been demonstrated to be the most effective enhancing MRI agent available at present. It is well tolerated and rapidly excreted. Using low concentrations and T_1 weighted IR and short TR, short TE spin echo pulse sequences, effective contrast enhancement can be achieved. Gd-DTPA enhancement was useful in identifying small tumours in the CNS which, because of similar relaxation times to those of normal brain, were not demonstrated on unenhanced MRI. It also provided information about the integrity of blood–brain barrier and in separating tumour from surrounding oedema. Complete assessment of lesions not accessible to direct CT imaging, such as spinal cord tumours and lesions obscured by calcifications, could benefit from the use of MRI with Gd-DTPA enhancement.

Most of the indications for contrast medium-enhanced MRI of CNS tumours are similar to those described for CT. However, the high soft-tissue contrast available with MRI enables some lesions not seen on CT to be identified. Contrast medium studies should be restricted to situations where non-enhanced MRI scans are negative but the clinical evidence of a tumour is strong, or in cases where additional information is needed for further management.

REFERENCES

Bloch, F., Hansen, W. W. & Packard, M., 1946. The nuclear induction experiment. *Physiologic Review, 70*, 474–485.

Bloembergen, N., Purcell, E. M. & Pound, R. V., 1948 Relaxation effects in nuclear magnetic resonance absorption. *Physics Review, 73*, 679–710.

Brant-Zawadzki, M., Badami, J. P., Mills, C. M., Norman, D. & Newton, T. H., 1984. Primary intracranial tumor imaging: a comparison of magnetic resonance and CT. *Radiology, 150*, 435–440.

Brasch, R. C., 1983 Work in progress: method of contrast enhancement for NMR imaging and potential applications *Radiology, 147*, 781–788.

Brasch, R. C., Weinmann, H. J. & Wesbey, G. E., 1984. Contrast enhanced NMR imaging: animal studies using gadolinium-DTPA complex. *American Journal of Roentgenology, 142*, 625–630.

Bydder, G. M., Steiner, R. E., Young, I. R., Hall, A. S., Thomas, D. J., Marshall, J., Pallis, C. A. & Legg, N. J., 1982. Clinical NMR imaging of the brain: 140 cases. *American Journal of Roentgenology, 139*, 215–236.

Bydder, G. M., Pennock, J. M., Steiner, R. E., Orr, J. S., Bailes, D. R. & Young, I. R., 1984. The NMR diagnosis of cerebral tumors. *Journal of Magnetic Resonance in Medicine, 1*, 5–29.

Bydder, G., Kingsley, D. P. E., Brown, J., Niendorf, H. P. & Young, I. R., 1985a. Magnetic resonance imaging of meningiomas, including studies with and without gadolinium-DTPA. *Journal of Computer Assisted Tomography, 9*, 690–697.

Bydder, G. M., Brown, J., Niendorf, H. P. & Young, I. R., 1985b Enhancement of cervical intraspinal tumors in MR imaging with intravenous gadolinium-DTPA. *Journal of Computer Assisted Tomography, 9*, 847–851.

Caille, J. M., Guibert-Tramier, F., Calabet, A., Billerey, J. & Piton, J., 1980. Abnormal enhancement after contrast injection. In *Computerized Tomography*. Ed. by J. M. Caille & G. Salamon (Springer-Verlag, Berlin), pp. 166–171.

Carr, D. H., Brown, J., Bydder, G. M., Weinmann, H. J., Speck, U., Thomas, D. J. & Young, I. R., 1984a. Intravenous chelated gadolinium as a contrast agent in NMR imaging of cerebral tumours. *Lancet, i*, 484–486.

Carr, D. H., Brown, J., Bydder, G. M., Steiner, R. E., Weinmann, H. J., Speck, U., Hall, A. S. & Young, I. R., 1984b. Gadolinium-DTPA as a contrast agent in MRI. initial clinical experience in 20 patients. *American Journal of Roentgenology, 143*, 215–224.

Carr, D. H., Brown, J., Leung, A. W.-L. & Pennock, J. M., 1984c. Iron and gadolinium chelates as contrast agents in NMR imaging: preliminary studies. *Journal of Computer Assisted Tomography, 8*, 385–389.

Curati, W. L., Graif, M., Kingsley, D. P. E., Niendorf, H. P. & Young, I. R., 1986. Magnetic resonance imaging: contrast enhancement of acoustic neuromas with intravenous gadolinium-DTPA. *Radiology, 158*, 447–451.

Damadian, R., 1971. Tumor detection by nuclear magnetic resonance. *Science, 171*, 1151–1153

Damadian, R., Zaner, K., Hor, D., Dimaio, T., Minkoff, L. & Goldsmith, H., 1973. Nuclear magnetic resonance as a new tool in cancer research: human tumors by NMR. *Annals of the New York Academy of Sciences, 222*, 1048–1076.

Felix, R., Schoerner, W., Claussen, C., Fiegler, W. & Niendorf, P., 1984 Diagnostic value of gadolinium-DTPA in imaging brain tumors. *Radiology*, 153, 84.

Gadian, D. G., 1982. *Nuclear Magnetic Resonance and its Application in Living Systems*. (Clarendon Press, Oxford), pp 159–183.

Gadian, D. G., Payne, J. A., Bryant, D. J., Young, I. R., Carr, D. H. & Bydder, G. M., 1985 Gadolinium-DTPA as a contrast agent in MR imaging—theoretical projections and practical observations *Journal of Computer Assisted Tomography, 9*, 242–251.

Graif, M., Bydder, G. M., Steiner, R. E., Niendorf, H. P., Thomas, D. G. & Young, I. R., 1985. Contrast enhanced MRI in malignant brain tumor. *American Journal of Neuroradiology, 6*, 855–862

Hazlewood, C. F., Cleveland, G. & Medina, D., 1974. Relation between hydration and proton nuclear magnetic relaxation times in tissue of tumor-bearing and non tumor-bearing mice: application for cancer detection. *Journal of the National Cancer Institute, 52*, 1849–1853.

Hollis, D. P., Economou, J. C., Parks, L. C., Eggleston, J. C. & Czeisler, J. L., 1973. Nuclear magnetic resonance studies of several experimental and human malignant tumors. *Cancer Research, 33,* 2156–2160.

Inch, W. R., McCredie, J. A., Krispel, R. R., Thompson, R. T. & Pintar, M. M., 1974 Water content and proton spin relaxation time for neoplastic and non neoplastic tissues from mice and humans. *Journal of the National Cancer Institute, 52,* 353–356

Lee, B. C. P., Kneeland, J. B., Walker, R. W., Posner, J. B., Cahill, P. T. & Deck, M. D. F., 1985. MR imaging of brainstem tumors. *American Journal of Neuroradiology, 6,* 159–163.

MacKay, J. M, Bydder, G. M. & Young, I. R., 1985. Magnetic resonance imaging of central nervous system tumors which do not display evidence of an increase in T_1 or T_2. *Journal of Computer Assisted Tomography, 9,* 1055–1061.

Mendonca-Dias, H. M., Gaggelli, E. & Lauterbur, P. C., 1983. Paramagnetic contrast agents in nuclear magnetic resonance medical imaging. *Seminars in Nuclear Medicine, 13,* 364–376

Mills, C. H., Crooks, L. E., Kaufman, L. & Brant-Zawadzki, M., 1984. Cerebral abnormalities: use of calculated T_1 and T_2 magnetic resonance images for diagnosis. *Radiology, 150,* 87–94.

Modic, M. T, Weinstein, M. A., Pavlicek, W., Boumphrey, F., Starnes, D. & Duchesneau, P. M., 1984. Magnetic resonance imaging of the cervical spine: technical and clinical observations. *American Journal of Neuroradiology, 5,* 15–22

Norman, D., Mills, C. M., Brant-Zawadzki, M., Yeates, A., Crooks, L. E. & Kaufman, L., 1984. Magnetic resonance imaging of the spinal cord and canal: potentials and limitations. *American Journal of Neuroradiology, 5,* 9–14.

Partain, C. L., Price, R. R, Patton, J. A., Stephens, W. H., Stewart, R. G. & James, A. E., 1983. The physical basis for NMR imaging In *Nuclear Magnetic Resonance Imaging.* Ed. by L C. Partain, A. E. James, F. D. Rollo & R. R. Price (W. B. Saunders, Philadelphia), pp. 60–72.

Pople, J. A., Schneider, W. G. & Bernstein, H. J., 1959. *High Resolution Nuclear Magnetic Resonance* (McGraw-Hill, New York), p. 209.

Pullan, B. R., Ritchings, R T. & Isherwood, I., 1981. Accuracy and meaning of computed tomography attenuation values. In *Radiology of the Skull and Brain,* Vol 5, *Technical Aspects of Computed Tomography.* Ed. by T. H. Newton & D G. Potts (C. V. Mosby, St Louis), pp. 3904–3917.

Pykett, I. L., Newhouse, J. H., Buonanno, F. S., Brady, T. J, Goldman, M R., Kistler, J P & Pohost, G. M., 1982. Principles of NMR imaging. *Radiology, 143,* 157–168.

Randell, C. P., Collins, A. G. A., Young, I. R., Hayward, R., Thomas, D. J., McDonnell, M. J, Orr, J. S., Bydder, G. M. & Steiner, R. E., 1983. Nuclear magnetic resonance imaging of posterior fossa tumors, 1983. *American Journal of Neuroradiology, 4,* 1027–1034. *American Journal of Roentgenology, 141,* 489–496.

Rosen, B. R. & Brady, T. J., 1983. Principles of magnetic resonance for medical application. *Seminars in Nuclear Medicine, 13,* 308–318.

Runge, V. M., Clanton, J. A., Lukehart, C. M., Partain, C L & James, E. A., 1983. Paramagnetic agents for contrast enhanced NMR imaging: a review *American Journal of Roentgenology, 141,* 1209–1215.

Sage, H. R., 1982. Blood brain barrier: phenomenon of increasing importance to the imaging clinician. *American Journal of Neuroradiology, 3,* 127–138.

Sarayan, L. A., Hollis, D. P., Economou, J. S & Eggleston, J. C., 1974. Brief communication: nuclear magnetic resonance studies of cancer. IV Correlation of water content with tissues relaxation times. *Journal of the National Cancer Institute, 52,* 599–602.

Schonner, V. W., Felix, R., Laniado, M., Lange, L., Weinmann, H. J., Claussen, C., Fiegler, W., Speck, V. & Kazner, E., 1984. Prufung des kernspintomographischen kontrast mittles Gadolinium-DTPA a.m. Munchen. *Fortschritte auf dem Gebiete der Röntgenstrahlen, 140,* 495–500.

Taylor, D. G. & Bore, C. F., 1981. A review of the magnetic resonance response of biological tissue and its applicability to the diagnosis of cancer by NMR radiology. *Computed Tomography, 5,* 122–133.

Weinmann, H. J., Brasch, R. C., Press, W. R. & Wesbey, G E., 1984. Characteristics of gadolinium-DTPA complex: a potential NMR contrast agent. *American Journal of Roentgenology, 142,* 619–624.

Young, I. R., Burl, M., Clarke, G. T., Hall, A. S., Passmore, T., Collins, A. G., Smith, D. T., Orr, J. S., Bydder, G. M., Doyle, F. H., Greenspan, R. H. & Steiner, R. E., 1981a. Magnetic resonance properties of hydrogen: imaging the posterior fossa. *American Journal of Roentgenology, 137,* 895–901.

Young, I. R., Clarke, G. J., Bailes, D R, Pennock, J. M., Doyle, F. H. & Bydder, G. M., 1981b. Enhancement of relaxation rate with paramagnetic contrast agents in NMR imaging. *Computed Tomography, 5,* 543–547.

Young, I. R., Bailes, D. R., Burl, M., Collins, A. G., Smith, D. T., McDonnell, M. J., Orr, J. S., Banks, L M, Bydder, G. M., Greenspan, R H & Steiner, R. E., 1982. Initial clinical evaluation of a whole body nuclear magnetic resonance (NMR) tomograph. *Journal of Computer Assisted Tomography, 6,* 1–18,

Zatz, C., 1981. Basic principles of computed tomography scanning In *Radiology of the Skull and Brain,* Vol. 5, *Technical Aspects of Computed Tomography.* Ed. by T. H. Newton & D. G. Potts (C V. Mosby, St Louis), pp. 3853–3876.

Zimmerman, R. D., Fleming, C. A., Saint-Louis, L., Lee, B. C. P., Manning, J. J., Deck, M. D., 1985. Magnetic resonance imaging of meningiomas. *American Journal of Neuroradiology, 6,* 149–157.

Book reviews

Atlas of Positron Emission Tomography of the Brain By W-D. Heiss, C. Beil, K. Herholz, G Pawik, R. Wagner and K. Weinhard, pp. ix + 116 + index, 1985 (Springer-Verlag, Berlin, Heidelberg), DM 148.
ISBN 3–540–15636–4

This atlas provides a brief account of the use of positron emission tomography in the study of cerebral function. The text, written in both German and English, covers the more important features of the technique. The first three chapters deal with the historical aspects, physics and radiochemistry of PET. Chapter 4 deals with the use of rubidium-82 and gallium-68 EDTA in assessing blood–brain barrier (BBB) integrity but contains nothing about other useful tracers that may be used to assess BBB function. The next three chapters deal with cerebral blood flow and the metabolism of oxygen and glucose. Tracer production, kinetic modelling and clinical uses are dealt with succinctly. Both normal and pathological brain are well documented The account of the latter includes cerebrovascular disease, epilepsy, dementia, movement disorders, psychiatric conditions and tumours Chapter 8 covers the concept of labelling amino-acids and the quantification of their uptake and incorporation into protein. The remaining chapters deal with the determination of cerebral pH, imaging receptor density and the selective visualisation of tumours.

The main criticism (which is difficult to direct at an atlas) is that with so many colourful illustrations, most of which are appropriately scaled, the reader may forget that the single most important aspect of PET is its ability to quantify biological processes in absolute units. PET complements rather than competes with CT scanning by providing useful information on cerebral *function*.

This book succeeds in filling a gap between the rather diverse journal articles and specialised textbooks on the subject. It should be of interest to clinicians and scientists not working directly in the field who wish for an up-to-date, easily readable pictorial review of the technique and clinical applications. It will be a useful addition to any postgraduate library.

R. P. BEANEY

Exercises in Radiological Diagnosis. Radiodiagnosis of the Skull. By Jean-Louis Dietemann, pp. vii + 168, 1985 (Springer Verlag, Berlin, Heidelberg, New York, Tokyo), DM.35.
ISBN 3–540–13266–X
0–387–13266–X

Radiodiagnosis of the Skull is a small volume which will enhance the series "Exercises in Radiological Diagnosis" from Professor Wackenheim's School of Radiology in Strasbourg.

The author, Jean-Louis Dietemann, is an experienced teacher and the book is well produced in a soft cover. Half is devoted to numbered radiographs, many of which are scaled to fill half a page. Almost all are sufficiently well produced to show detail and all demonstrate a well chosen principle. The other half contains correspondingly numbered, clear, line diagrams. Each is accompanied by a suitable, but limited, clinico-pathological commentary which, almost without exception or printing error, is particularly well translated by Marie-Therese Wackenheim. References are limited but it is obvious that the author has both interest and experience with lesions which deform the image of the sella turcica

Now that CT is so well established, it is important to understand the contribution of conventional skull radiography. This book will be of personal value to all needing instruction to interpret skull radiographs. It will certainly educate towards correct diagnosis and, therefore, self confidence. It can be carried easily in the pocket and used unobtrusively in front of viewing screens. The axiom, "Radiological changes should always be interpreted in the light of clinical data" eventually appears on page 131, Case 60.

If his book encourages the trainee to collect a series of similar radiographs and to elaborate briefly the commentary with words chosen personally from additional sources, then Jean-Louis Dietemann will have certainly achieved his ambition. This commendable little learning aid takes its place alongside a comparable publication on the vertebrae.

G. HART

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The cricopharyngeus revisited

By Olle Ekberg, M.D.

Department of Diagnostic Radiology, Malmö General Hospital, S-214 01 Malmö, Sweden

(*Received November 1985*)

ABSTRACT

The motor function of the pharyngo-oesophageal (PO) segment during swallowing in terms of tonicity, relaxation and peristalsis was evaluated in 25 patients with a posterior cricopharyngeus impression. Functional abnormalities were common. Defective tonicity was present in 11 patients. Relaxation was normal in all patients except at the level of the cricopharyngeal muscle. Abnormal peristalsis was present in 19 patients as weakness, paresis or abnormal timing. The impression of the cricopharyngeus was effaced during the late stage of swallowing due to collapse proximal and distal to the cricopharyngeus. It was not due to successive distension at the level of the cricopharyngeus. In 11 patients there was some retention of barium proximal to the cricopharyngeus after the passage of the barium bolus. This was due to weakness in the inferior pharyngeal constrictor and/or an abnormal timing of the peristalsis whereby contraction of the cricopharyngeus occurred before peristalsis in the inferior pharyngeal constrictor had cleared the pharynx of barium. The observations indicate that bulging of the cricopharyngeal muscle is only one aspect of a profoundly altered motor function of the PO segment.

In patients with swallowing complaints cineradiography has revealed abnormal function in the majority of patients (Ekberg & Nylander, 1982a). In 25% of patients with dysphagia there is abnormal relaxation of the cricopharyngeal muscle seen as a posterior impression in the pharyngo-oesophageal (PO) segment (Ekberg & Nylander, 1982b). The motor function of the PO segment can be divided into three distinct functions, namely tonicity between swallowing, relaxation at the initiation of swallowing and peristalsis for conveying the bolus material into the oesophagus.

The aim of the present investigation was to analyse the motor function of the PO segment in terms of tonicity, relaxation and peristalsis in patients with bulging of the cricopharyngeal muscle, using a cineradiographic technique.

PATIENTS AND METHODS

Twenty-five patients with dysphagia who had a posterior impression due to the cricopharyngeal muscle during swallowing were selected at random. They were examined using a 35 mm cineradiographic technique. The patients were examined in the erect position with at least two antero-posterior and two lateral series (Figs 1–3) while swallowing a mouthful of barium contrast medium. Radiographs were obtained at a speed of 50 frames/s.

Tonicity within the PO segment was graded as normal, weak or defective. Relaxation in the PO segment was graded as normal or defective. The abnormal relaxation of the cricopharyngeal muscle was categorised as either delayed or defective. Peristalsis was registered at three levels, namely inferior pharyngeal constrictor, cricopharyngeal muscle and cervical oesophagus, respectively, and was graded as normal, weak or paretic. Abnormal timing was also noted. The presence or absence of barium retention above the cricopharyngeal muscle was also noted. For statistical analysis, Student's *t*-test was used.

RESULTS

Tonicity in the inferior pharyngeal muscle was normal in 21 patients, weak in two and absent in another two patients. The tonicity was normal in all patients at the level of cricopharyngeal muscle. Tonicity in the cervical oesophagus was normal in 14, weak in six and absent in five patients.

The relaxation of the PO segment was normal except for the level of the cricopharyngeal muscle. At this level the gullet rapidly attained almost its maximum width concurrently with the segments above and below. However, during the late stage of bolus passage there was an additional distension of the cricopharyngeal level. This increase in width varied between 0 and 7 mm (mean 2 mm). Such an increase in width was registered in 17 patients while the width was unaltered in seven and decreased in one patient.

Peristalsis in the inferior pharyngeal constrictor was normal in 12, weak in nine and absent in three patients. There was defective timing in 13 patients. Peristalsis was normal in 23 patients at the level of the cricopharyngeal muscle, weak in one and absent in one patient. Peristalsis was normal in the cervical oesophagus in 16 patients, weak in seven and absent in two. In four patients there was abnormal timing of peristalsis in the cervical oesophagus.

There was retention of barium at the level of the inferior pharyngeal contrictor immediately cranial to the cricopharyngeal muscle in 11 patients. This retention was due to weak or paretic peristalsis within the inferior pharyngeal constrictor and defective timing, that is, contraction of the cricopharyngeal muscle prior to peristalsis in the caudal part of the inferior pharyngeal constrictor in eight of the patients, while in

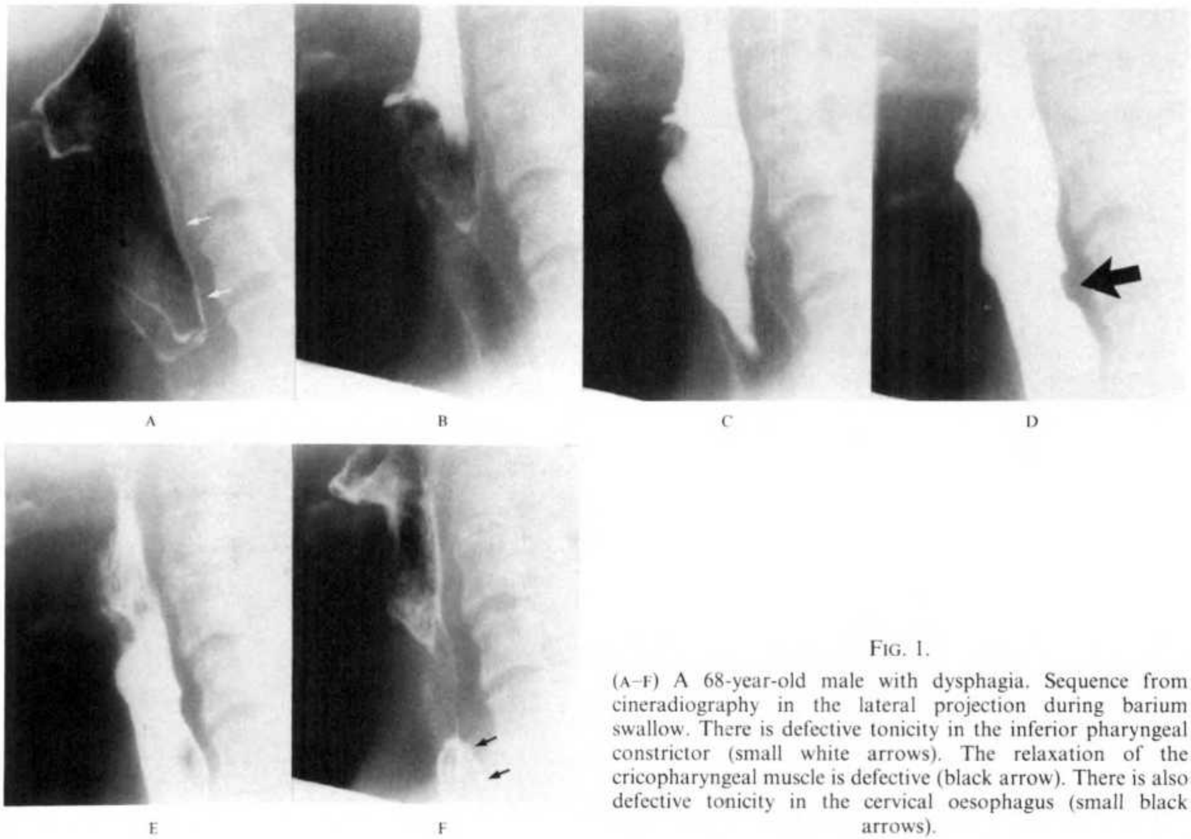

FIG. 1.

(A–F) A 68-year-old male with dysphagia. Sequence from cineradiography in the lateral projection during barium swallow. There is defective tonicity in the inferior pharyngeal constrictor (small white arrows). The relaxation of the cricopharyngeal muscle is defective (black arrow). There is also defective tonicity in the cervical oesophagus (small black arrows).

three there was only weak peristalsis in the inferior pharyngeal constrictor.

DISCUSSION

The PO segment is located between the pharynx cranially and the cervical oesophagus caudally. Morphological abnormalities within the PO segment, such as diverticula of Zenker's and Kilian-Jamieson's types, are of great clinical importance (Seaman, 1969; Ekberg & Nylander, 1982a, 1983; Goyal, 1984). Dysfunction in this area is commonly described as spasm of the cricopharyngeal muscle (Ellis, 1971; Ekberg & Nylander, 1982b; Curtis et al, 1984; Goyal, 1984; Torres et al, 1984). By detailed cineradiographic analysis of the motor function of the PO segment it is possible to obtain a better understanding of the pathophysiology of abnormalities in this region.

The relaxation of the cricopharyngeal muscle has been described as either delayed or defective in patients with a posterior impression (Ekberg & Nylander, 1982b). Delayed relaxation was present when the impression disappeared during the late stages of barium passage while defective relaxation was present when an impression was seen throughout the passage of the barium bolus. This study indicates that when the posterior impression due to the cricopharyngeus was effaced during the late phase of pharyngeal swallowing (delayed relaxation), this was not due to a widening of the lumen at the level of cricopharyngeus, but rather was due to collapse of adjacent pharynx and oesophagus. This implies that, in patients with a persistent bulging of the cricopharyngeus throughout the act of swallowing, this merely reflects lack of contractility in the proximal and distal segments. This might be due to muscular weakness or, when pronounced, to paresis.

The peristaltic wave at the level of the inferior pharyngeal constrictor (thyropharyngeal muscle) was frequently abnormal. This was partly registered as a premature contraction in the cricopharyngeus. The latter muscle, however, contracted at the correct moment, that is, as if peristalsis had passed uninterrupted through the inferior pharyngeal constrictor. This relatively premature closure of the cricopharyngeus gave a varying degree of proximal bolus retention in the pharynx corresponding to a pseudodiverticulum (Ekberg & Nylander, 1982b). However, in some patients there was also a delay in the peristaltic contraction within the cervical oesophagus caudal to the cricopharyngeus.

The observations indicate that in patients with an impression due to the cricopharyngeal muscle there is a

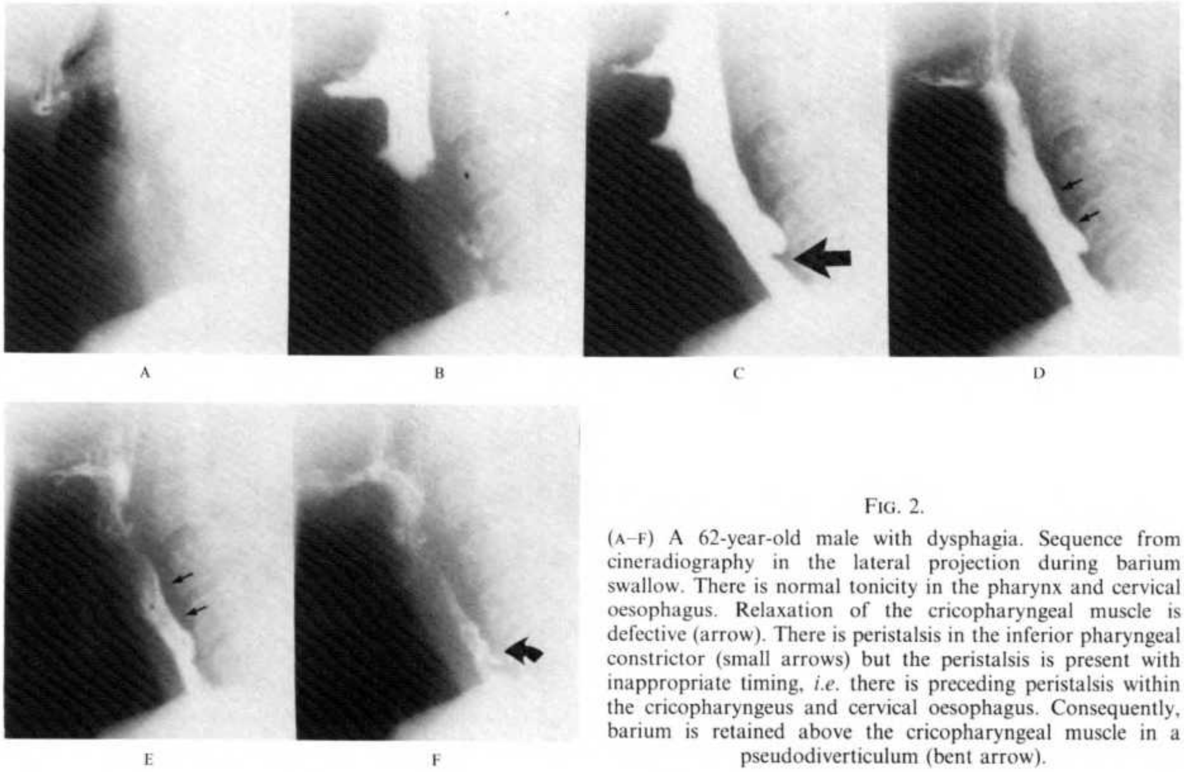

FIG. 2.

(A–F) A 62-year-old male with dysphagia. Sequence from cineradiography in the lateral projection during barium swallow. There is normal tonicity in the pharynx and cervical oesophagus. Relaxation of the cricopharyngeal muscle is defective (arrow). There is peristalsis in the inferior pharyngeal constrictor (small arrows) but the peristalsis is present with inappropriate timing, *i.e.* there is preceding peristalsis within the cricopharyngeus and cervical oesophagus. Consequently, barium is retained above the cricopharyngeal muscle in a pseudodiverticulum (bent arrow).

more widespread and pronounced dysfunction in the PO segment. This is frequently seen as defective peristalsis or tonicity in the inferior pharyngeal constrictor and/or in the cervical oesophagus. The nature of such a dysfunction in the PO segment could not be further evaluated from this study. Efferent motor control of the PO segment, and especially of the cricopharyngeus, is controversial (Kirschner, 1958; Lund & Ardran, 1964; Lund, 1965; Doty, 1968; Murakami et al, 1972; Helemans & Vantrappen, 1974; Miller, 1982; Goyal, 1984). The somatic efferent motor control from the nucleus ambiguus via the tenth and eleventh cranial nerves is agreed, whereas consensus is lacking about the contribution of sympathetic and parasympathetic innervation. Other aspects of innervation of the PO segment are poorly understood. Abnormalities within the medulla oblongata or efferent nerves or in the pharyngeal plexus covering the constrictor muscles of the pharynx may be responsible for abnormal motor function. However, lesions in the precentral gyrus, which is the cortical representation of swallowing, or in the pathway between the cortex and the medulla (the first motor neuron) have to be considered (Doty, 1968; Ellis, 1971; Miller, 1982; Goyal, 1984).

Tonicity of the PO segment is important for sealing off the oesophagus from the pharynx and thereby hindering regurgitation. All patients had normal tonicity in the cricopharyngeal muscle. Four patients with defective tonicity in the cricopharyngeal muscle have been reported earlier (Ekberg et al, 1985). Such a defective tonicity, *per se*, probably does not cause symptoms.

Retention of barium at the level of the inferior pharyngeal constrictor above the cricopharyngeal muscle was common and was due to a combination of weak peristalsis in the inferior constrictor and abnormal timing evident as a low speed of peristalsis through the inferior pharyngeal constrictor. Such retention has been observed in these patients and referred to as pseudodiverticulum (Ekberg & Nylander, 1982b). It might be presumed that such a pseudodiverticulum should have pathological importance in the development of a Zenker's diverticulum. However, such a transition has never been observed. It is probable that a Zenker's diverticulum requires additional anatomical prerequisites to develop. The relation between age and different pharyngo-oesophageal abnormalities have been reported (Ekberg & Wahlgren, 1985) and showed clearly the different correlation with age between a defective relaxation of the cricopharyngeal muscle and Zenker's diverticulum. There is, therefore, no simple correlation between defective relaxation of the cricopharyngeal muscle and the development of a Zenker's diverticulum.

From the results of this study, the earlier description

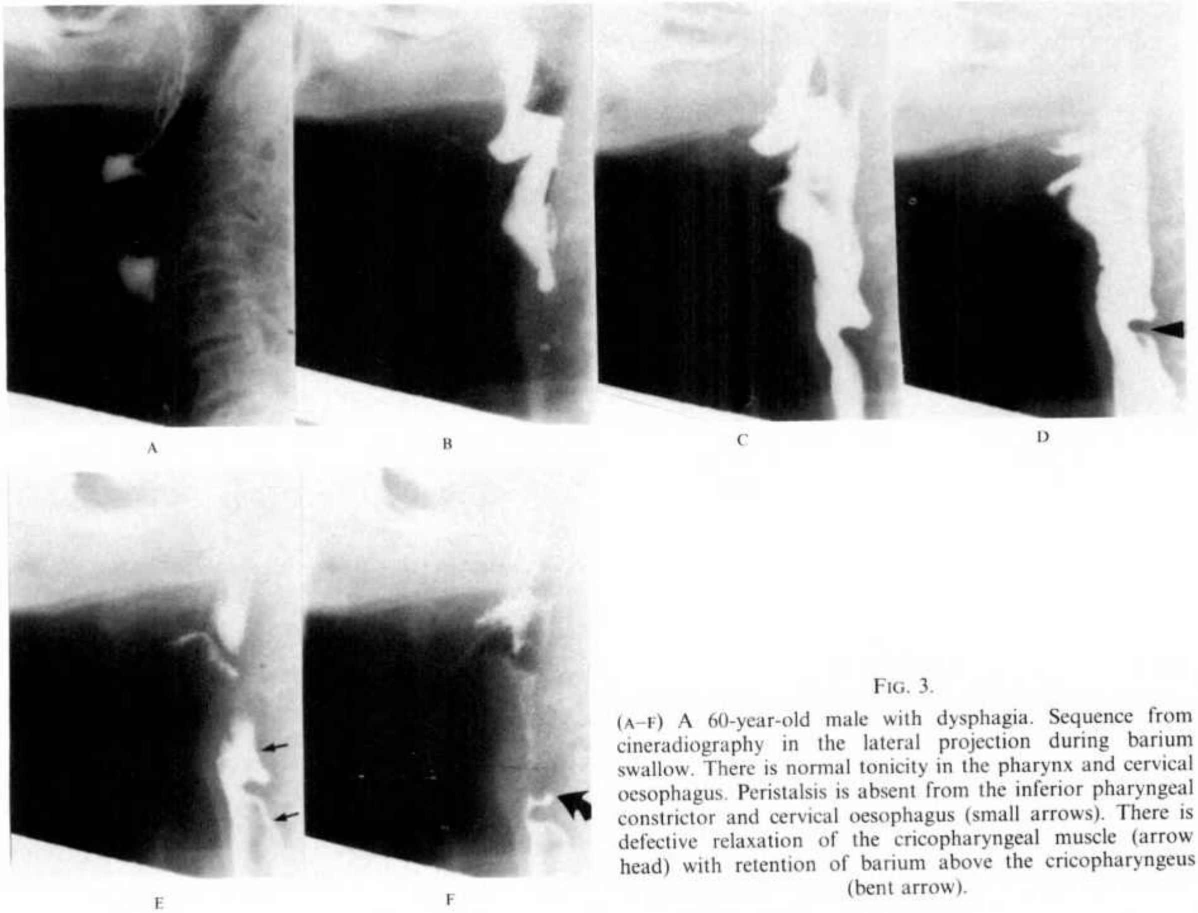

FIG. 3.

(A–F) A 60-year-old male with dysphagia. Sequence from cineradiography in the lateral projection during barium swallow. There is normal tonicity in the pharynx and cervical oesophagus. Peristalsis is absent from the inferior pharyngeal constrictor and cervical oesophagus (small arrows). There is defective relaxation of the cricopharyngeal muscle (arrow head) with retention of barium above the cricopharyngeus (bent arrow).

of cricopharyngeus dysfunction in terms of delayed and defective relaxation ought to be omitted. The abnormal relaxation of the cricopharyngeal muscle is only one aspect of incoordinated motor function in the PO segment, but cricopharyngeal impression is probably the most important sign of this dysfunction. Moreover, cricopharyngeus impression and pseudodiverticulum are conspicuous and easy to recognise.

REFERENCES

CURTIS, D. J., CRUESS, D. F. & BERG, T., 1984. The cricopharyngeal muscle: a videorecording review. *American Journal of Roentgenology*, *142*, 497–500.

DOTY, R. W., 1968. Neural organization of deglutition. *Handbook of Physiology, Alimentary Canal* (American Physiological Society, Washington DC), Section 6, Vol. 4, Chap. 92, pp. 1861–1902.

EKBERG, O., LINDGREN, S. & NYLANDER, G., 1985. Chalasia of the upper esophageal sphincter. *Acta Radiologica Diagnosis*, *26*, 557–561.

EKBERG, O. & NYLANDER, G., 1982a. Cineradiography of the pharyngeal stage of deglutition in 250 patients with dysphagia. *British Journal of Radiology*, *55*, 258–262.

EKBERG, O. & NYLANDER, G., 1982b. Dysfunction of the cricopharyngeal muscle. A cineradiographic study in patients with dysphagia. *Radiology*, *143*, 481–486.

EKBERG, O. & NYLANDER, G., 1983. Lateral diverticula from the pharyngoesophageal junction area. *Radiology*, *146*, 117–122.

EKBERG, O. & WAHLGREN, L., 1985. Dysfunction of pharyngeal swallow. A cineradiographic study in 854 dysphagial patients. *Acta Radiologica Diagnosis*, *26*, 389–395.

ELLIS, F. H., 1971. Upper esophageal sphincter in health and disease. *Surgical Clinics of North America*, *82*, 553–565.

GOYAL, R. K., 1984. Disorders of the cricopharyngeus muscle. *Otolaryngologic Clinics of North America*, *17*, 115–131.

HELEMANS, J. & VANTRAPPEN, G., 1974. The pharyngoesophageal sphincter. *Diseases of the Esophagus* (Springer-Verlag, Berlin), pp. 40–58.

KIRSCHNER, J. A., 1958. The motor activity of the cricopharyngeus muscle. *Laryngoscope*, *68*, 1119–1159.

LUND, W. S., 1965. The function of the cricopharyngeal sphincter during swallowing. *Acta Otolaryngologica*, *59*, 497–510.

LUND, W. S. & ARDRAN, G. M., 1964. The motor nerve supply of the cricopharyngeal sphincter. *Annales d'Otolaryngologie*, *73*, 599–617.

MILLER, A. J., 1982. Deglutition. *Physiology Reviews*, *62*, 129–184.

MURAKAMI, Y., FUKUDA, H. & KIRSCHNER, J. A., 1972. The cricopharyngeus muscle. An electrophysiological and neuropharmacological study. *Acta Otolaryngologica Supplementum, 311*, 5–19.

SEAMAN, W. B., 1969. Functional disorders of the pharyngeal-esophageal junction. Achalasia and chalasia. *Radiologic Clinics of North America, 7*, 113–119.

TORRES, W. E., CLEMENTS, J. L., AUSTIN, G. E. & KNIGHT, K., 1984. Cricopharyngeal muscle hypertrophy: radiologic–anatomic correlation. *American Journal of Roentgenology, 141*, 927–930.

Book review

Manual of Clinical Magnetic Resonance Imaging. Ed. by J. P. Heiken, H. S. Glazer, J. K. T. Lee, W. A. Murphy and M. Gado, pp. 110, 1986 (Raven Press, New York), $21.00. ISBN 0-88167-167-3

Intended for both radiographers and radiologists as a practical guide to performing magnetic resonance imaging (MRI) in the head and body, this manual has been written by radiologists from the USA with a number of years' experience in MRI. It is divided into two main sections, with an introduction to the technical aspects including a clear and concise account of the physical principles, imaging techniques and some of the common artefacts encountered. This is followed by guidelines for conducting an MR examination in the form of protocol tables. These tables list separate imaging sequences covering different anatomical sites within various regions of the body and, also, in some instances, different pathologies. The pulse sequences chosen are all varieties of spin-echo. There is a useful comments section to each table explaining the rationale for selection of the imaging parameters and for altering the examination, depending on the circumstances. An explanation is given of the operator-control (machine) parameters used in the protocol tables together with a summary of safety aspects and patient preparation. Selected references (up to 1985) and an index are included.

This is a readable, basic introduction into the technical aspects of MRI. The protocol tables are not meant to be followed rigidly but are intended as a guide, as machine parameters will vary with different MRI systems. Despite the fact that the strategies are intended for MRI systems using field strength magnets of 0.3 T or more, they are applicable even for lower field systems. Overall the tables indicate a good approach but there is no mention of the inversion-recovery sequence, which can be useful in certain instances. A short account of the different operator handling requirements and types of magnet systems in use would have been informative.

The manual, being pocket sized with a metal spiral binding, is good value. It can be recommended to radiographers and radiologists and would be especially useful for those starting out in MRI.

J. P. R. JENKINS

Book reviews

Endourology. Ed. by Culley C. Carson and N. Reed Dunnick, pp xii+315+index, 1985 (Churchill Livingstone, Edinburgh), £55.00.
ISBN 0-443-08367-3

The transformation that has taken place over the last 5 years for the treatment of calculous disease in the urinary tract seems to have popularised a new term, "endourology". The editors define endourology as a subspeciality embracing aspects of general urology, urological surgery, urological radiology and interventional radiology, terms perhaps more familiar and understandable. The fact that the contributors to the book are predominantly radiologists and urologists bears testament to the close co-operation needed to practise endourology with success and this book details the initial radiological steps required before urologists can use endoscopy in the renal tract and manipulate within it. Indeed, it is the endoscopic removal of renal and ureteric calculi that forms the basis of this book.

To gain access to the kidney's collecting system requires a precise knowledge of renal anatomy, specifically its vascular component. The first chapter deals admirably with this. Subsequent chapters detail the methods available for the removal of both renal and ureteric stones and describe the various methods of disintegration of stones that cannot be removed in one piece. Ultrasound lithotripsy and electrohydraulic lithotripsy are well covered. From the contributors' vast experience in this field come manoeuvres for getting at and removing those stones in seemingly impossible situations, which those just setting up a service or those with only moderate experience will find of value. The role of chemolysis and of extracorporeal shock-wave lithotripsy in stone disease is covered. In the middle of the book comes a chapter on percutaneous nephrostomy and renal drainage techniques. Important though these techniques are, it seems a little out of place and it is interesting that its author describes endourology as interventional radiology.

The development of lasers for use in the urinary tract for both the treatment of calculous disease and tumour is covered. Potential complications of endourology and their treatment are discussed. Importantly, there is a chapter devoted to the paediatric patient but no mention of endoscopic diagnostic ultrasound is made, a modality which should fall within the scope of this book.

For those embarking on percutaneous renal surgery and the treatment of calculous disease in the urinary tract, this book provides a wealth of experience to draw upon. It is well written, well illustrated and reasonably priced. It should be on the shelves of both radiology and urology departments where renal calculous disease is not treated with a 12-inch incision.

David Rickards

Ovarian Cancer. Ed. by N. M. Bleehen, pp. x+140+index, 1985 (Springer-Verlag, Berlin, Heidelberg, New York, Tokyo), DM.148.
ISBN 0-540-13326-7

This small, well produced book contains summaries of the principal papers presented at the 6th Royal College of Radiologists' Symposium (1984) on this difficult subject. Potential readers should not be deterred by the 2-year gap between the meeting and the availability of the book. A number of the papers are well worth reading for their clear accounts of different facets of the subject. The difficult subject of the pathology is refreshingly clearly discussed by Anderson, while the surgery (Scott) and the use of radiological techniques (Johnson) for diagnosis and staging are presented in balanced review. The enormous experience of the Charing Cross group is well represented by Bagshawe's extensive summary of tumour markers and the group's experience on the chemotherapy of the rare malignant germ cell tumours.

Two rather long chapters address the problems of the place of radiotherapy (Bush) and chemotherapy in multicentre studies (Guthrie). Bush himself wonders during this representation of the Princess Margaret Hospital (PMH) data why the conclusion of the original PMH study on post-operative radiotherapy in high-risk patients has been slow to gain acceptance. Perhaps that is the question he should have addressed himself to in this review. The potentially bewildering role of chemotherapy discussed by Guthrie presents a historical review whose relevance has been overtaken by time and new agents. There are a number of chapters in this book that justify its place in an oncology library.

R Hunter

1986, *The British Journal of Radiology*, 59, 881–885 SEPTEMBER 1986

Computed tomography of abdominal carcinoid tumour

By *M. Gould, F.R.C.R. and R. J. Johnson, B.Sc., M.B.B.S., M.R.C.P., F.R.C.R.
Christie Hospital & Holt Radium Institute, Wilmslow Road, Withington, Manchester M20 9BX

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ABSTRACT

Ten patients with pathologically proven abdominal carcinoid tumour were assessed by computed tomography (CT). Post-mortem examination correlation was obtained in two cases. Computed tomography demonstrated the extent of intra-abdominal tumour well and is, therefore, a useful staging technique for patients being treated with adjuvant therapy. The appearances of metastatic carcinoid within the mesentery on CT are characteristic and can enable a pre-operative diagnosis to be made.

Several isolated reports of the appearance on computed tomography (CT) of metastatic carcinoid tumour to the small bowel mesentery have been described (Bernardino et al, 1979; Seigel et al, 1980; Whitley et al, 1982). More recently, the spectrum of intra-abdominal disease has been documented (McCarthy et al, 1984; Picus et al, 1984; Cockey et al, 1985). We report here the appearances on abdominal CT in 10 patients, with post-mortem correlation in two of these.

PATIENTS AND METHODS

Ten patients, with ages ranging from 37 years to 79 years were referred to a regional oncology centre with metastatic abdominal carcinoid tumour. Pathological confirmation had been obtained in nine cases at laparotomy and in one by lymph-node biopsy. The primary tumour had been resected at surgery in five patients. Presenting symptoms had been abdominal pain in six patients, an abdominal mass in three and supraclavicular lymphadenopathy in one.

Abdominal CT scans were performed at the time of referral on an EMI 7070 scanner using a 3 s scan time. One centimetre-thick contiguous sections were obtained through the liver with alternate 1 cm-thick sections from below this level to the anterior superior iliac spines. All patients had been given 250 ml of 5% sodium diatrizoate/meglumine diatrizoate (Gastrografin, Schering AG) 12 h, 3 h and 15 min before scanning. Immediately prior to scanning patients were given 0.5 mg hyoscine butylbromide (Buscopan, Boehringer Ing.) intramuscularly as a smooth-muscle relaxant. No intravenous contrast enhancement was used. Follow-up scans were obtained during treatment. There were a total of 33 scans on these 10 patients and all were reviewed and assessed for extent of intra-abdominal disease with particular reference to involvement of the liver, mesentery, lymph nodes and bowel. In two patients information from a post-mortem study could be correlated with a recent CT scan.

RESULTS

The various sites of involvement for individual patients are detailed in Table I. The appearances on CT at the site of involvement are detailed below. The appearances described are those seen on the first CT scan.

Primary site

The primary tumour had been resected in six patients before referral. Computed tomography failed to detect it in the remaining four. In one of these an ileo-caecal tumour was found at the post-mortem examination.

Mesentery

The commonest appearance within the mesentery, occurring in eight patients (80%), was of a soft-tissue-density mass measuring between 0.5 cm and 5 cm in diameter. There were linear soft-tissue densities radiating from the mass in all cases. Calcification was seen within the mass in two patients (Figs 1, 2).

Other rounded soft-tissue densities, thought to represent discrete nodes, were seen in six patients (60%). These varied in size from 0.25 cm to 1 cm (Fig. 2).

Lymph nodes

Nodes greater than 1.5 cm in diameter in the retroperitoneum and 0.6 cm in diameter in the retrocrural space were considered abnormal. Using these criteria retroperitoneal lymphadenopathy was seen in six patients (60%) and retrocrural lymphadenopathy in one.

Liver metastases

Focal hypodense lesions were seen in six patients (60%). Two of these patients had clinical and biochemical evidence of the carcinoid syndrome.

Bowel involvement

In six patients (60%) diffuse small-bowel wall thickening (greater than 0.3 cm) was noted. These thickened loops were seen always in association with a mesenteric mass (Fig. 3).

Other sites

An ovarian mass was seen in one patient and an omental mass in another. These were biopsy-proven

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*Present address: Colchester General Hospital, Turner Road, Colchester CO4 5JL.

carcinoid metastases. Ascites was seen in five patients (50%).

Follow-up abdominal CT examination

In all patients there was evidence of progression of disease with increase in size of the mesenteric mass (Figs 1, 2), development of ascites or increase in the size and number of liver metastases. Three patients died during the course of follow-up and a post-mortem examination was performed in two of these (Cases 2 and 8).

At post-mortem examination, tumour was found at all abnormal sites on CT. Computed tomography delineated the extent of mesenteric and retroperitoneal disease particularly well. In Case 2, CT failed to demonstrate several small hepatic serosal metastases and in Case 8 a small primary tumour in the ileo-caecal angle was not seen. Some of the findings related to Case 2 are illustrated in Figs 4–7.

DISCUSSION

Carcinoid tumour is the commonest small-bowel tumour, 90% originating in the terminal ileum. Most primary lesions are discovered incidentally at surgery or autopsy and measure less than 1.5 cm in diameter. Invasion and spread of tumour from the primary site are accepted indicators of malignancy rather than more usual histological criteria such as anaplasia and mitotic frequency (Godwin, 1975). The patients presenting with symptoms related to the tumour usually have advanced disease. The primary tumour is slow growing, rarely causing symptoms until it has spread through the bowel wall, peritoneum and into the mesentery. Tumour spread is related to the size of the primary lesion occurring in 80% of patients with lesions greater than 2 cm in diameter but in only 2% of patients with lesions less than 1 cm in diameter. Mesenteric infiltration evokes a fibroblastic reaction in the mesentery and surrounding small bowel. This results in loops of bowel becoming matted together, kinking and buckling on their mesenteric border. This is thought to produce the commonest symptom, pain, due to intermittent intestinal obstruction. As the malignant process spreads the mesenteric lymph nodes become involved, often producing a palpable mass. Further tumour spread to the root of the mesentery may encase the vessels and produce mesenteric infarction (Case 4 in this series) (Moertel et al, 1961).

The primary tumour is rarely demonstrated radiologically (Moertel et al, 1961; Jeffree et al, 1984, Picus et al, 1984) and this was our experience in those

TABLE I

DETAILS OF PATIENTS

Case/ age (years)/ sex	Signs/ symptoms	Carcinoid syndrome	Primary site		Miscellaneous sites	CT appearances					
			known	unknown		Liver metastases	Mesentery		Ascites	Bowel-wall thickening	Retroperitoneal lymphadenopathy
							mass	nodes			
1/37/M	Abdominal pain, anaemia	+		+		−	+	+	−	+	+
2/54/M	Diarrhoea, weight loss	−	Terminal ileum			−	Calcified	−	+	+	+
3/61/M	RIF mass	−	Caecum			+	+	−	−	−	−
4/79/F	Abdominal pain	+		?Small bowel ?Ovary		+	+	+	−	−	−
5/47/F	Pelvic mass, small-bowel obstruction	−	Terminal ileum			+	+	+	−	+	−
6/62/M	Abdominal pain	−	Terminal ileum			−	+	+	+	+	+
7/51/F	Abdominal pain	−		+	Omentum	+	−	−	+	−	−
8/49/F	R supra-clavicular lymph node	−	Terminal ileum		Ovary	+	+	−	+	+	+
9/52/M	RIF mass, diarrhoea, abdominal pain	+	Caecum			+	−	−	+	−	+
10/63/M	Abdominal pain, diarrhoea, nausea	−		+		−	Calcified	+	−	+	+

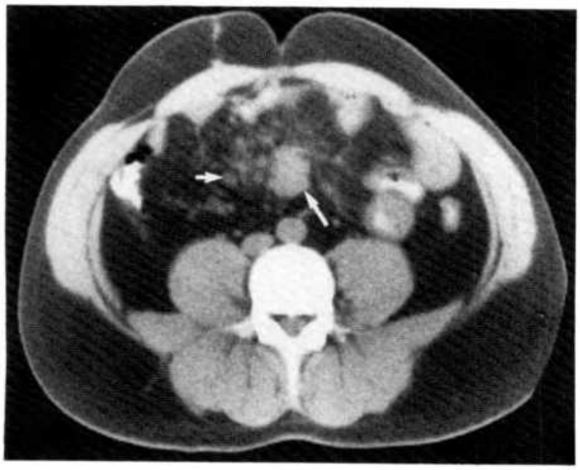

FIG. 1.

Computed tomography scan demonstrating an irregular mesenteric mass (large arrow) with radiating linear densities. Smaller rounded masses (small arrow), representing discrete enlarged lymph nodes, can also be seen.

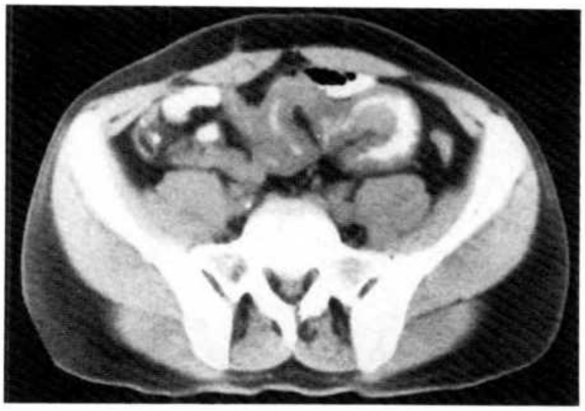

FIG. 3.

Computed tomogram demonstrating small-bowel loops with thickened walls and consequent attenuation of the contrast column.

patients with a primary lesion *in situ*.

Mesenteric involvement can be demonstrated on barium studies with fixation and separation of bowel loops (Balthazar, 1978; Jeffree et al, 1984). Angiography may demonstrate mesenteric vessel involvement. Computed tomography is a useful non-invasive technique for assessing the extent of mesenteric involvement (McCarthy et al, 1984; Picus et al, 1984; Cockey et al, 1985). The typical appearances have been demonstrated in this series. The commonest finding, occurring in 80% of patients, is of a soft-tissue-density mass associated with linear soft-tissue densities radiating from it. This mass may be associated with thickened bowel loops, apparently adherent to the mass, and also extend to the root of the mesentery encasing the proximal mesenteric vessels (Figs 1–3). Post-mortem examination in two patients demonstrated a firm mass in the mesentery with tangled loops of small bowel adherent to it. The mass extended superiorly around the mesenteric vessels. Histology revealed the mass to be a combination of fibrosis and tumour. The radiating soft-tissue densities shown on CT were due to tumour infiltration and fibrosis of the neurovascular bundles (Figs 4–7).

The appearances on CT of mesenteric involvement by carcinoid tumour are characteristic and unlikely to be confused with other disease processes. Well defined, rounded, soft-tissue-density masses within the

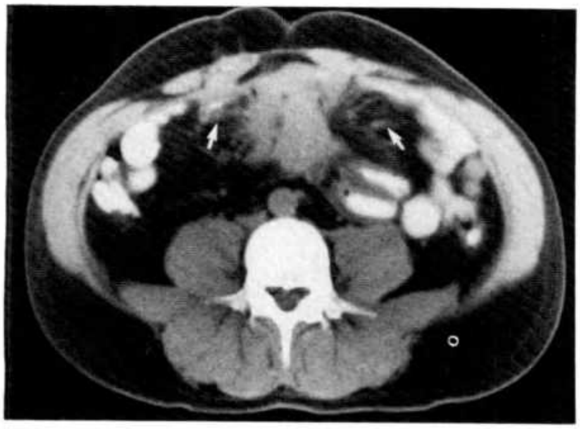

FIG. 2.

A later CT scan in the same patient as Figure 1 demonstrating an increase in size of the mesenteric mass, now containing calcification. The associated linear densities (arrows) are well seen and represent neurovascular bundles thickened by tumour and fibrosis.

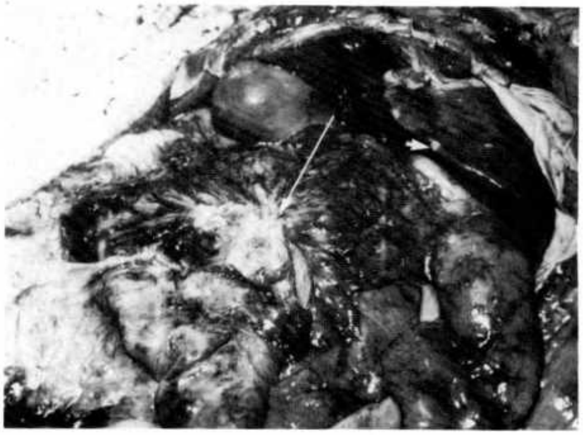

FIG. 4. *Case 2.*

Post-mortem photograph demonstrating a mesenteric mass of tumour and fibrosis (long arrow) with radiating bands of thickened neurovascular bundles. Serosal metastases on the left lobe of the liver are also seen (short arrow).

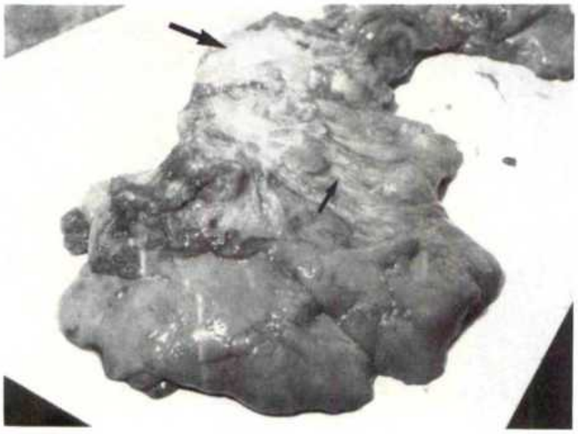

FIG. 5. *Case 2.*

Post-mortem photograph of the detached mesentery and small bowel demonstrating the mesenteric mass (large arrow) and neurovascular bundles (small arrow) thickened by tumour and fibrosis.

mesentery can be seen in lymphoma, leukaemia and metastatic carcinoma, often from the ovary, and sarcoma, frequently leiomyosarcoma. Diffuse, ill-defined masses can also be seen in these conditions and in carcinoma of the colon, stomach and pancreas when they may represent contiguous tumour spread. Mesenteric lymphadenopathy has recently been reported in Kaposi's sarcoma (Moon et al, 1984). A "stellate" appearance of the mesentery may be seen in peritoneal mesothelioma and metastatic carcinoma from many primary sites.

However, in contradistinction to carcinoid, in all these conditions it is unusual to see a combination of all three appearances. Also there may be clinical evidence of the primary tumour and other features on the CT scan, not seen in carcinoid, to indicate the diagnosis.

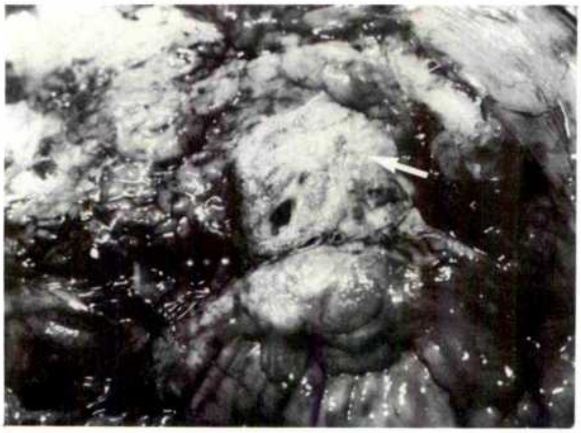

FIG. 6. *Case 2.*

Post-mortem photograph demonstrating extension of tumour to the root of the mesentery (arrow).

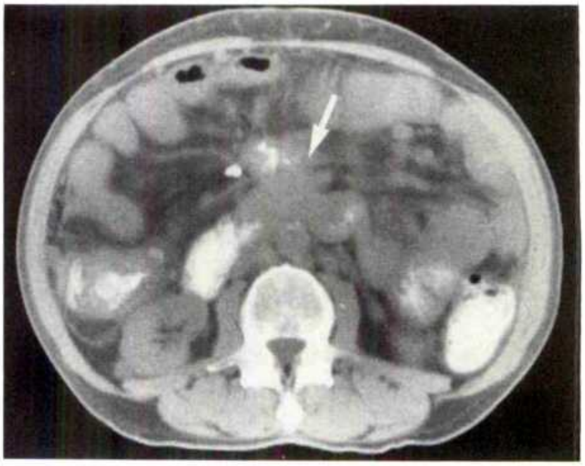

FIG. 7. *Case 2.*

Computed tomogram demonstrating the mesenteric mass within the root of the mesentery (arrow) and the thickened neurovascular bundles.

Mesenteric abnormalities can be seen in benign disease. Bowel-wall thickening associated with mesenteric changes has been reported in Crohn's disease. However, rounded masses are unusual (Cockey et al, 1985). The condition which may cause most confusion with carcinoid is the very rare entity of retractile mesenteritis (Seigel et al, 1980).

At presentation, between 50% and 85% of patients with carcinoid have regional lymph-node metastases (Moertel et al, 1961). Detection of enlarged nodes by CT in this condition was first described by Picus et al (1984), retroperitoneal lymphadenopathy occurring in 35% of their patients. In this series retroperitoneal lymphadenopathy occurred in 60% of patients. Limitations of CT scanning mean that metastases in normal-sized nodes will not be identified and, therefore, some patients will be incorrectly staged. Recently, retroperitoneal fibrosis and nodes secondary to carcinoid tumour within the body of the pancreas have been documented (Gupta et al, 1985). The retroperitoneal fibrosis had surrounded the abdominal aorta, inferior vena cava and right renal artery causing renovascular hypertension.

Liver metastases at presentation are common and occurred in 60% of our patients. The findings on CT of focal hypodense lesions were non-specific, as reported in other series (Sako et al, 1982; Picus et al, 1984). In this series the liver metastases had been confirmed at surgery, while follow-up scans showed an increase in size and number of the liver lesions. Detection of liver metastases by CT is related to scanning technique; 1 cm-thick contiguous sections through the liver increase the detection rate (Johnson et al, 1983; Picus et al, 1984). Limitations of the technique mean that small lesions (less than 1 cm in diameter) may be missed. In one of our patients serosal liver metastases less than 0.5 cm in diameter, observed at post-mortem examination, had not been identified on the CT scan.

In conclusion, while CT is poor at detecting the primary lesion it is reliable in assessing the extent of tumour spread within the abdomen. Surgery is the treatment of choice and few patients are diagnosed before laparotomy. However, increasing numbers of patients have adjuvant therapy and CT would appear to be the investigation of choice in obtaining baseline observations prior to treatment and in assessing response, as the sites of metastases are difficult areas to assess clinically.

In patients with unexplained abdominal pain, the characteristic CT findings described above may be diagnostic.

ACKNOWLEDGMENTS

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REFERENCES

Balthazar, E. J., 1978. Carcinoid tumours of the alimentary tract. *Gastrointestinal Radiology, 3*, 47–56.

Bernardino, M E., Jing, B. S. & Wallace, S., 1979. Computed tomography diagnosis of mesenteric masses. *American Journal of Roentgenology, 132*, 33–36.

Cockey, B. M , Fishman, E. K., Jones, B. & Siegelman, S S., 1985. Computed tomography of abdominal carcinoid tumour. *Journal of Computer Assisted Tomography, 9*, 38–42.

Godwin, J. D , II, 1975. Carcinoid tumours An analysis of 2837 cases. *Cancer, 36*, 560–569.

Gupta, A., Saibil, F , Kassim, O. & McKee, J., 1985. Retroperitoneal fibrosis caused by carcinoid tumour. *Quarterly Journal of Medicine, 56*, 367–375.

Jeffree, M. A., Baxter, S. J., Hemingway, A. P. & Nolan, D. J., 1984. Primary carcinoid tumours of the ileum: radiological appearances *Clinical Radiology, 35*, 451–455.

Johnson, R. J., Blackledge, G., Eddleston, B. & Crowther, D., 1983. Abdomino-pelvic computed tomography in the management of ovarian carcinoma. *Radiology, 146*, 447–452.

McCarthy, S. M , Stark, D. D , Moss, A. A. & Goldberg, H I., 1984. Computed tomography of malignant carcinoid disease *Journal of Computer Assisted Tomography, 8*, 846–850

Moertel, C. G., Sauer, W. G., Dockerty, M. B. & Baggenstoss, A. H., 1961. Life history of the carcinoid tumour of the small intestine. *Cancer, 14*, 901–912

Moon, K. L., Jr, Federle, M. P., Abrams, D. I., Volberding, P. & Lewis, B. J., 1984. Kaposi sarcoma and lymphadenopathy syndrome: limitations of abnormal CT in acquired immunodeficiency syndrome. *Radiology, 150*, 479–483.

Picus, D , Glazer, H. S., Levitt, R. G. & Husband, J. E., 1984. Computed tomography of abdominal carcinoid tumours. *American Journal of Roentgenology, 143*, 581–584.

Sako, M., Lunderquist, A., Owman, T., Martensonn, H. & Nobin, A., 1982. Angiographic and computed tomographic appearances of secondary carcinoid of the liver. *Cardiovascular Interventional Radiology, 5*, 90–96.

Seigel, R. S , Kuhns, L. R , Borlaza, G. S., McCormick, T. L & Simmons, J. L., 1980. Computed tomography and angiography in ileal carcinoid tumour and retractile mesenteritis. *Radiology, 134*, 437–440.

Whitley, N. O., Bohlman, M. E. & Baker, L. P., 1982. CT patterns of mesenteric disease. *Journal of Computer Assisted Tomography, 6*, 490–496

Book reviews

Arterial Variations in Man. Classification and frequency. By H. Lippert and R. Pabst, pp 121, 1985 (J. F. Bergmann Verlag, Munich), 65 DM (approx. £20)
ISBN 3–8070–0341–X (Munich)
0–387–00341–X (New York)

Professors Lippert and Pabst of the Anatomy Department of the Hanover Medical School have collected 676 references to the varying patterns of arterial distribution in humans from both anatomical and radiological sources. They have distilled this information into a compact, clear and comprehensive book which gives diagrams in red of the distribution of arteries in every area of the body, together with a percentage frequency of occurrence, a brief description and the relevant references.

As the authors point out, the normal textbook pattern of vascular distribution may be present in only a proportion of the population. Radiologists and surgeons are aware of the commoner variations, but until now have had no readily available source of information about the variations in the whole arterial tree. This book will become an essential accompaniment for every angiographer and the authors are to be congratulated on the clarity with which they present so much complex information.

W. D. Jeans

Aortitis. Clinical, pathologic and radiographic aspects. Ed. by Adam Lande, Yahya M. Berkmen, and Hugh A. McAllister Jr, pp. x+269, 1986 (Raven Press, New York), $63.50.
ISBN 0–88167–141–X

This is a monograph on aortitis by 15 authors whose diverse backgrounds reflect the protean nature of their subject. Together with Takayasu's disease, the acute systemic phase of which is, surprisingly, claimed to be common in England and Scandinavia (p. 56), syphilis and mycotic aneurysms, there are descriptions of aortitis with rheumatic fever, rheumatoid arthritis and giant cell arteritis. There is a chapter on radiological aspects of aortitis by two of the editors which is superbly illustrated with more than 80 aortograms and nuclear magnetic resonance and computed tomographic scans. Other chapters cover medical, surgical and pathological aspects, and there are contributions from ophthalmologists, a neurologist and a paediatrician.

The volume brings together under one cover a mass of information that would otherwise be virtually impossible to obtain, and is comprehensively referenced. The authors point out that aortitis tends to be underdiagnosed because it is so uncommon in many clinician's practices compared with atherosclerosis. For those who feel vulnerable to the challenge of recognising the condition, this slim volume will make rewarding reading.

Roger N. Baird

1986, *The British Journal of Radiology*, 59, 887–894 SEPTEMBER 1986

Experimental evaluation of various available contrast agents for use in the gastrointestinal tract in case of suspected leakage. Effects on pleura

By Abida Z. Ginai

Department of Radiology, University Hospital Dijkzigt, Rotterdam, The Netherlands

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ABSTRACT

Intrapleural injections of seven contrast agents were carried out in experimental rats in order to find a safe contrast agent to use in the radiological examination of the upper gastrointestinal tract in cases where leakage outside the upper gastrointestinal tract into the pleural space could be suspected, particularly post-operatively. The contrast agent in such cases could enter the mediastinum, pleura, peritoneum or lungs and bronchi. Hexabrix (May and Baker) and Gastrografin (Schering AG) produced the least tissue reaction in the pleura. Due to the potential risk of aspiration in such cases Gastrografin is not suitable as it is known to produce significant reaction in the lungs and may even prove to be fatal. Hexabrix, therefore, appears to be the safest contrast agent where leakage into the pleural space may be suspected.

Experimental work was carried out to find a safe and suitable contrast agent for use in the gastrointestinal tract in cases where leakage outside the tract could be suspected, particularly post-operatively. The contrast agent used in the radiological evaluation of such cases can enter the mediastinum, pleura, or peritoneum, or be aspirated into the bronchi and lungs, or enter the lungs via a fistula. The reactions of various conventional gastrointestinal and bronchographic contrast agents as well as the more recent low-osmolality contrast agents metrizamide (Amipaque, Nycomed (UK) Ltd) and Hexabrix (May and Baker) have already been studied in the bronchi and lungs (Ginai et al, 1984), mediastinum (Ginai et al, 1985) and peritoneum (Ginai, 1985). This paper presents the effects of various contrast agents on the pleura of rats. Amipaque, which was used in the previous studies on lungs, mediastinum and peritoneum, is now replaced by iohexol (Omnipaque, Nycomed (UK) Ltd).

MATERIALS AND METHOD

One hundred and eight male rats (Wistar Strain, outbred stock, wu/cpb (Zeist, The Netherlands)), weighing between 264 g and 395 g were used. The rats were divided into nine main groups of 12 rats, seven groups receiving contrast agents (see below) and two control groups, one receiving physiological saline and the other anaesthetic only.

(1) Pure barium sulphate ~ 90% weight/volume (w/v) suspension.
(2) Micropaque, commercial barium sulphate suspension 100% w/v (Laboratories Nicholas Gaillard).
(3) Gastrografin, sodium and meglumine diatrizoate 370 mg I/ml (Schering AG, Berlin).
(4) Dionosil, aqueous suspension of *n*-propylester of 3 : 5-diiodo-4-oxopyridin-1-ylacetate (Glaxo Laboratories Ltd, Greenford, Middlesex).
(5) Hytrast, aqueous suspension of *N*-propyl-2 : 3 diol 3 : 5-diiodo-4-pyridone (NPP) and 3 : 5 diiodo-4-pyridone (DIP) (Guerbet Laboratories, Paris).
(6) Omnipaque, iohexol in a concentration of 350 mg I/ml (Nycomed (UK) Ltd).
(7) Hexabrix, meglumine and sodium ioxaglate 320 mg I/ml (May and Baker, Dagenham).
(8) Physiological saline, 0.9% sodium chloride solution.
(9) Control, anaesthetic only.

Each main group was further divided into three subgroups of four rats according to the day of sacrifice (1 day, 8 days and 42 days). The rats were anaesthetised with ether and then placed on a rat board. A small incision was made on the left chest wall laterally, usually between the fifth and the sixth ribs obliquely in the line of the ribs. The chest wall and intercostal muscles were carefully dissected until the parietal pleura was reached. Through a small opening in the pleura, which always caused an immediate pneumothorax, 0.2 ml (equal to ~ 45 ml in a 70 kg man) of one of the contrast agents or physiological saline was injected using a blunt polyethylene catheter. Immediately following the injection, the opening in the chest wall was closed with two or three layers of stitches. Radiographs of the chest were taken in the postero-anterior and lateral positions immediately after the injection and again on the day of sacrifice. In addition, radiographs were taken on Days 2 and 4 in the 8-day group and Days 7, 14 and 28 in the 42-day group. Subgroups of four animals from each main group were sacrificed (using an overdose of ether) at 1 day, 8 days and 42 days after receiving the contrast agent or saline. At dissection, the chest was carefully opened on both

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Address for correspondence and reprints: Dr A. Z. Ginai, Department of Radiology, University Hospital Dijkzigt, Dr Molewaterplein 40, 3015 GD Rotterdam, The Netherlands.

sides and examined for the presence and distribution of contrast agent, any pleural effusion present and any gross abnormalities of the lungs, mediastinum, diaphragm and chest wall. Biopsies were taken from both sides of the chest and consisted of: (a) at least two biopsies of the intercostal muscle with parietal pleural lining chosen randomly but excluding the region of surgery when visible; (b) the diaphragm; (c) the infracardiac mediastinal tissue consisting of a loose fatty type of tissue with pleural lining; and (d) sections from both lungs with visceral pleural lining. In addition, lymph nodes (paratracheal and anterior mediastinal where possible) in the 8-day and 42-day groups were also removed. All these tissues were immersed in formalin for about 2–4 weeks, after which histological sections were prepared and stained with haematoxylin and azophloxin. The histological evaluation was based on the type and severity of the inflammatory reaction. The presence or absence of contrast agent was also noted.

The histological reaction in the pleura was graded as follows: 0 no reaction; + mild reaction; ++ moderate reaction; +++ severe reaction. The χ^2 test (for K independent samples) was applied for the determination of the level of significance.

RESULTS

The animals, in general, tolerated the anaesthetic and the surgical procedure quite well. There were three deaths in total, all occurring following anaesthesia, before X-ray examination (see Table I). The general complications of surgery included three rib fractures, which healed well, and a total of nine animals in which the left lung was caught in the inner layer of chest wall stiches. In these animals adhesions were also seen between the left lung and the chest wall at the site of introduction of the contrast agent.

Radiological findings

All contrast agents were clearly visible on the chest radiographs taken immediately after injection. Despite the care taken to inject only into the left pleural space, the contrast agent was most often seen in both pleural spaces (Fig. 1A), sometimes only on the left side (Fig. 1B) but sometimes mainly on the right side (Fig. 1C). At this stage, pneumothorax was always present on the left side (Fig. 1). In the case of Omnipaque, Hexabrix, Gastrografin and Dionosil, the agent appeared to be almost completely absorbed after 24 h and in these groups, as well as the physiological saline group, there was no demonstrable pneumothorax on the 24 h radiographs. No recognisable collapse, consolidation or pleural effusion could be seen in these groups up to the 42nd day.

TABLE I

TISSUE REACTION IN THE PLEURA OF 108 RATS

Agent	Day of dissection			Total
	1	8	42	
Pure barium sulphate	++	+++	++	26
	++	+++	++	
	++	+++	–	
	++	+++	++*	
Micropaque	+++	+++	+++	33
	+++	+++	+++	
	++	++	+++	
	+++	++*	+++	
Hytrast	+++	++	+	23
	+++	++	+	
	+++	++	+	
	+++	++*	0	
Dionosil	+	++	+	11
	+	+	+	
	+	+	0	
	+	+	0	
Gastrografin	+	++	+	10
	+	++	+	
	+	+	0	
	0	0	0	
Omnipaque	++	++	+	13
	+	++	+	
	+	+	0	
	+	+	0	
Hexabrix	+	+	++	9
	+	+	+	
	0	+	+	
	0	0	0	
Physiological saline	+	+	+	5
	+	+	0	
	0	0	0	
	0	0	0	
Control	0	+	+	3
	0	0	+	
	0	0	0	
	0	0	0	
Total	47	52	34	

0 no reaction; + mild reaction; ++ moderate reaction; +++ severe reaction.
*Animals who died.
–Contrast agent not in pleura.

The pure barium sulphate, Micropaque and Hytrast groups showed definite localisation of the contrast agents in the region of the mediastinum, mainly to the left and anteriorly. Only very slight variations were seen up to the 42nd day in the pure barium sulphate and Micropaque groups (Fig. 2). The Hytrast group, however, showed only a tiny amount of residual contrast agent by the 42nd day. These three groups (pure barium sulphate, Micropaque and Hytrast) also appeared to have some pleural effusion on Day 1 and in some cases until Day 8. A small pneumothorax was also seen in many animals in these groups until this time. No contrast-filled lymph nodes could be defined in the mediastinal region on radiographs, but small areas suggestive of collapse/consolidation of the lungs were visible in some rats in all three groups.

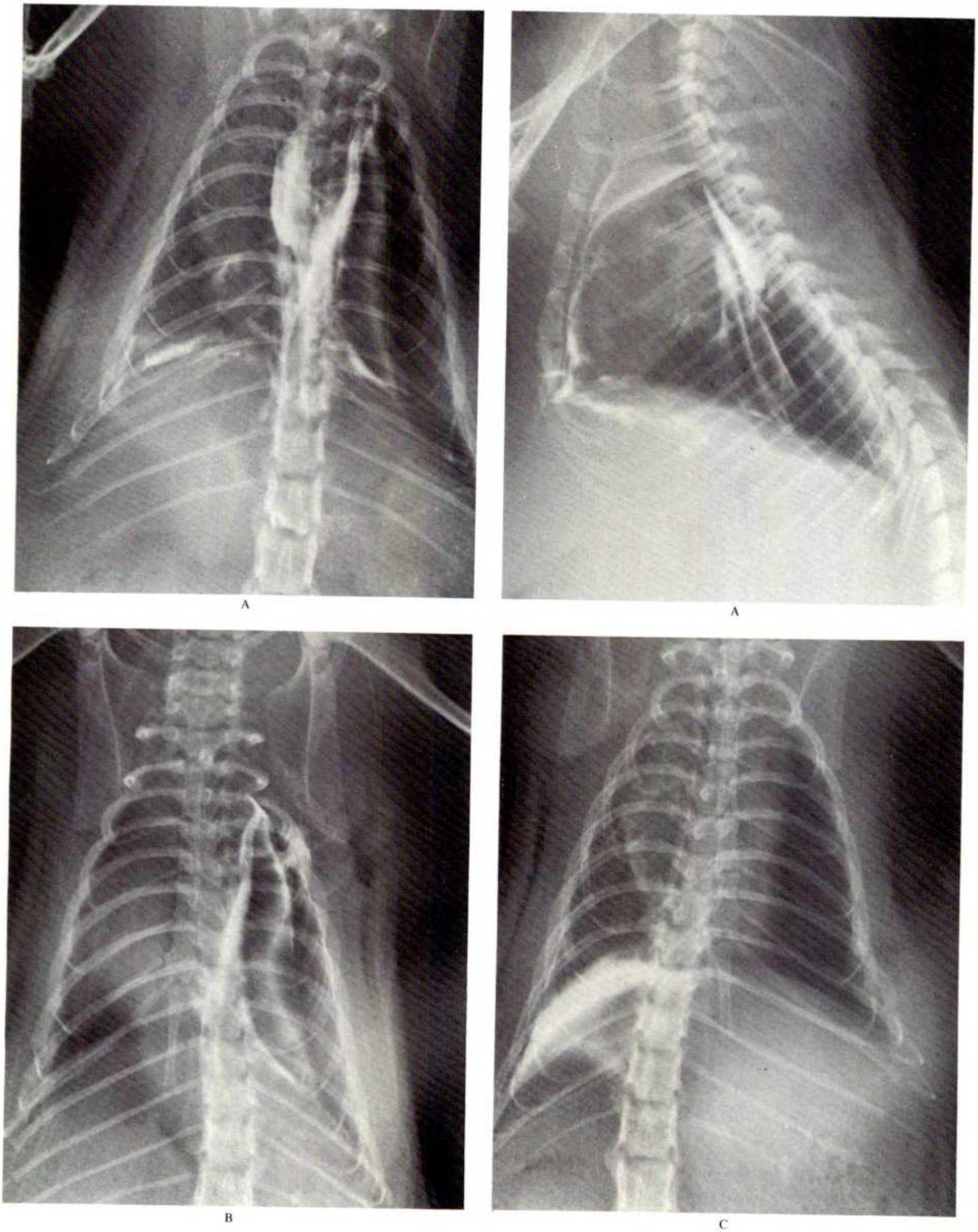

FIG. 1.

Radiographs taken immediately after introduction of contrast medium into pleura. (A) Postero-anterior and lateral radiographs of the chest showing Micropaque in the pleural spaces. (B) Hytrast visible only in the left pleural space with a left pneumothorax. (C) Hexabrix is seen to be mainly in the right pleural space with pneumothorax. A left pneumothorax is also visible.

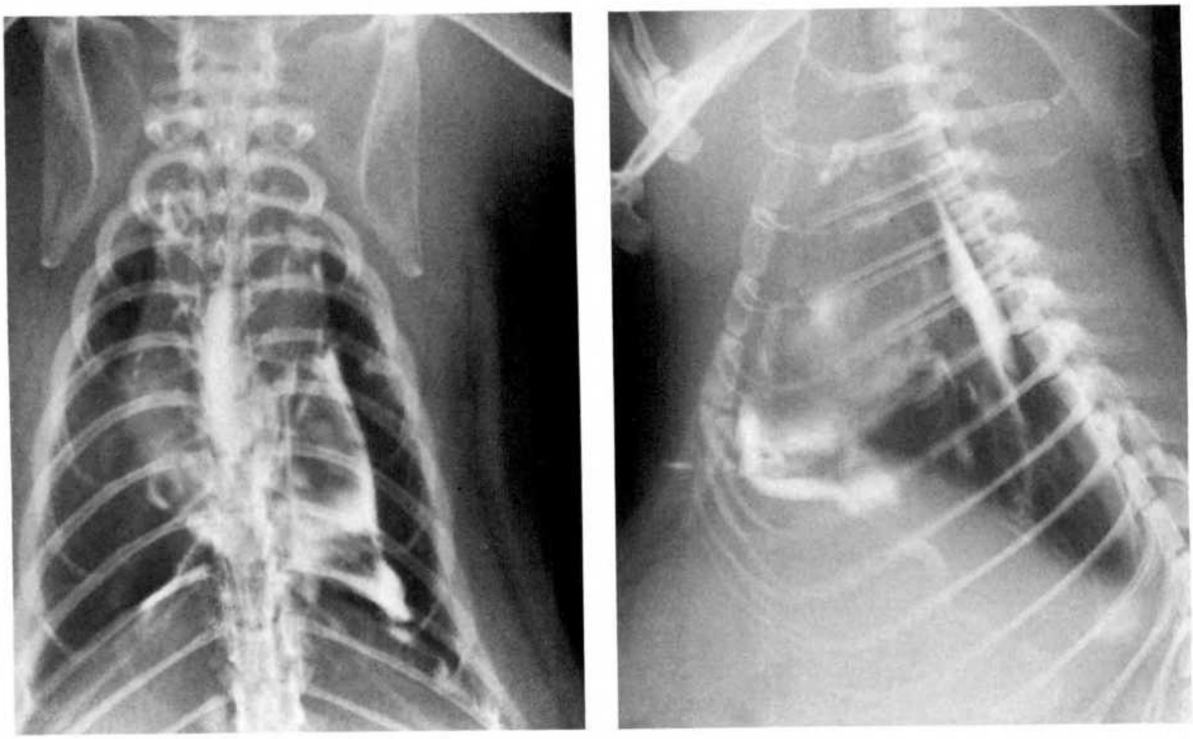

FIG. 2.

Postero-anterior and lateral radiographs taken 42 days after introduction of Micropaque (same rat as Fig. 1A). Very little change is in the quantity of contrast agent since the Day-1 radiographs (Fig. 1A).

Pathological findings

Gross examination. The gross abnormalities whenever present were always more marked on the side of injection (left side) than the right side of the chest. The chest wall wound appeared to be fully healed in the 8-day group.

Pure barium sulphate and Micropaque were seen as whitish plaques in places on the parietal pleural lining of the chest wall, on the pleural surface of the diaphragm and over the surface of the lung. The contrast agent appeared to collect mainly centrally in the loose connective tissue of the mediastinum, particularly in the infracardiac region. A slight to moderate pleural effusion, containing whitish contrast agent, was noted on Day 1 and the quantity of contrast agent on the left side was much more than on the right side of the chest. Adhesions were noted between the left lung and the mediastinum and to a lesser degree between the right lung and the mediastinum. These were most marked on Day 8, but also visible till Day 42. Areas of collapse/consolidation in the lungs were visible in some rats. Hytrast tended to clump, particularly in the mediastinal region, with moderate pleural effusion on Day 1: dark red areas were seen on the lung surfaces and in later stages some adhesions occurred between the lungs and the mediastinum. The quantity of contrast agent and number of adhesions were, however, considerably reduced by Day 42. The Omnipaque, Gastrografin, Hexabrix, Dionosil and physiological saline groups showed no detectable pleural effusion or any sign of contrast agent at any stage on dissection. No collapse or consolidation of the lungs was noted on gross examination, nor any adhesions between the lung and the mediastinum. Adhesions were seen occasionally between lung and parietal pleura at the site of the injection in those animals where the lung was accidentally caught in the chest-wall stitches (nine animals).

Histological reaction

The histological changes were, in general, almost always most significant on the left side but less marked changes were often also found on the right side, particularly intrapulmonary abnormalities.

Pure barium sulphate. The histological reaction was more marked on the left side. At Day 1, deposits of contrast agent were seen in the parietal pleural lining of the thoracic wall, diaphragm and the mediastinal structures, and was mostly superficial and extracellular. The most abundant collection of contrast agent was seen in the infracardiac mediastinal fat and its pleural lining (Fig. 3). This was accompanied by a fibrinous,

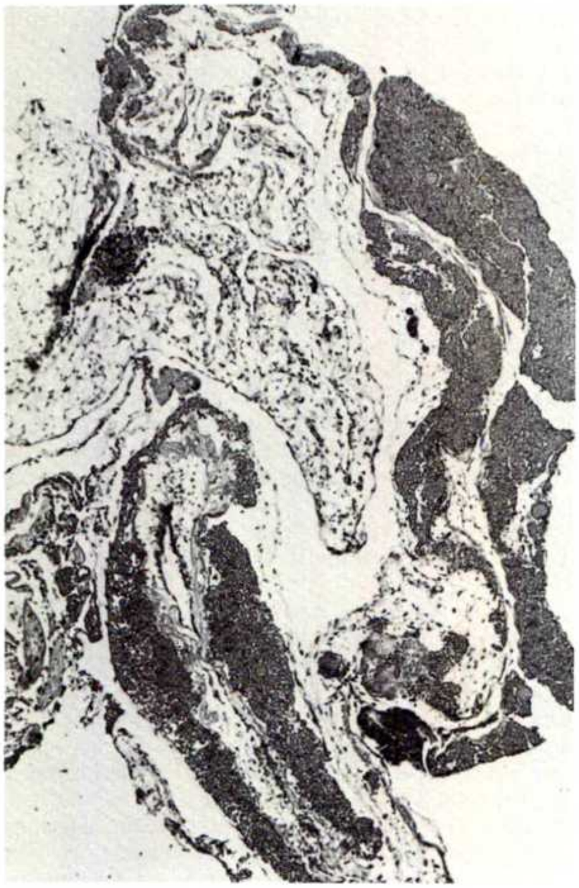

FIG. 3.

Histological section showing pure barium sulphate collections at Day 1 in the mediastinal infracardiac pleura and fatty tissue (haematoxylin and azophloxin, × 60).

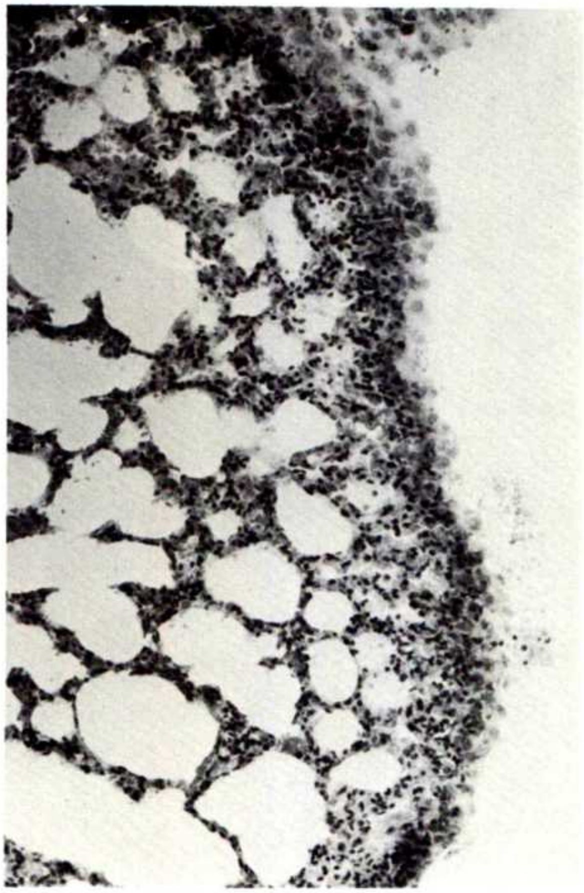

FIG. 4.

Histological section at Day 1 after Micropaque introduction, showing swelling and proliferation of visceral pleural mesothelial cells. No pulmonary parenchymal abnormalities are visible. (H & A, × 150).

histiocytic reaction with some polymorphonuclear cells. The visceral pleura covering the lung appeared swollen with small deposits scattered mainly over the surface and not intracellularly (Fig. 4).

On Day 8, the reaction of the parietal pleura was again most extensive in the mediastinal region, with much less change in the region of the diaphragm and chest wall. At this stage, extensive intracellular quantities of contrast agent were seen within the histiocytes with occasional multinucleated foreign-body giant cells. Similar but scattered reactions were also seen on the surface of the lung within the pleura.

At 42 days, extensive fibroblastic histiocytic infiltration was seen, with some lymphocytes and multinucleated giant cells in the parietal and visceral pleura (Fig. 5). The histiocytes were loaded with granular-looking contrast material. The reaction was most marked in the mediastinal fatty tissue and parietal pleura. In the lungs, small focal perivascular infiltrates were seen in most of the animals with lymphocytes, histiocytes, polymorphs and eosinophils in places. This reaction was similar in both lungs, although the pleural reaction was always more marked on the side of injection of the contrast agent.

Micropaque. Histological reaction in the pleura caused by Micropaque was very similar to that by pure barium sulphate except that at 42 days the mediastinal lymph nodes also showed accumulation of some of the contrast agent within the histiocytes.

Hytrast. On Day 1, extensive deposition of contrast-agent crystals was seen in the pleura, particularly the mediastinum with local necrosis accompanied by fibrinous deposits and polymorph infiltration. Swelling of the mesothelial lining cells was noted with infiltration of histiocytes. The visceral pleura covering the lung showed a diffuse reaction with swelling of the subpleural mesothelial cells and polymorphs. The contrast agent was particularly concentrated in the mediastinal region of the pleura. Intrapulmonary foci of

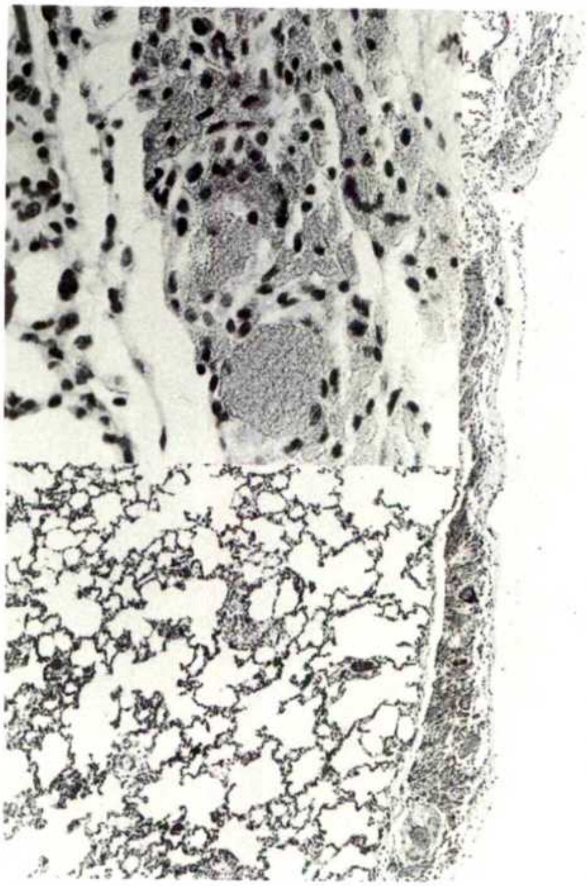

FIG. 5.

Histological section at 42 days after pure barium sulphate injection showing visceral pleura with extensive granulomatous reaction with intracellular barium sulphate collections in histiocytes and multinucleated giant cells (H & A, × 60, inset H & A, × 380).

inflammatory reaction were also noted with small areas of collapse of the lung in places.

On Day 8, extensive fibrohistiocytic reaction with central necrosis was seen. Intracellular contrast-agent crystals were also seen in the histiocytic cells and multinucleated, foreign-body giant cells. The visceral pleura showed focal thickening with subpleural infiltration containing lymphocytes and eosinophils. Both lungs showed perivascular lymphocytic infiltrations with some eosinophils.

At Day 42, the pleural reaction was similar to that at Day 8 but less severe. The lymph nodes showed follicular lymphoid hyperplasia but no contrast agent was present.

Dionosil. On Day 1, swelling of the lining cells of the parietal pleura was seen with slight diffuse reaction with some histiocytes and polymorphs in places; polymorphonuclear infiltration was also evident in the visceral pleura.

On Day 8, a fibrotic reaction was observed, with thickening of the parietal pleura and infiltration with histiocytes, polymorphs and eosinophils; on the visceral surface, there was focal proliferation of the subpleural tissue.

On Day 42, there was slight swelling of mesothelial cells of the parietal pleura with some fibrosis. Slight thickening of the visceral pleura was also seen in places, while subpleural and perivascular infiltrates with mononuclear cells were noted in both lungs at all stages, *i.e.* at 1 day, 8 days and 42 days.

Omnipaque. On Day 1, slight polymorphonuclear reaction with swelling of the mesothelium was noted in the parietal pleura. The visceral pleura showed some swelling of the cells with a slight inflammatory reaction. On Day 8, there was minimal reaction in the parietal pleura with slight subpleural and intrapulmonary infiltration with lymphocytes and histiocytes. On Day 42, a minimal reaction was seen similar to that of Day 8.

Hexabrix. On Day 1, swelling of the connective tissue was present in the mesothelium of the parietal pleura and a little fibrinous exudate was present in the visceral pleura of two animals. No intrapulmonary abnormality was seen. At Day 8, swelling of the parietal pleural mesothelium was seen with some plasma cells, histiocytes and eosinophils present. The visceral pleura showed some increase in the mesothelial stroma and there was slight intrapulmonary perivascular infiltration with polymorphs, histiocytes and lymphocytes. The lymph nodes showed follicular lymphoid hyperplasia. At Day 42 a similar reaction as at Day 8 was seen, except that there were no changes in the lymph nodes.

Gastrografin. On Day 1, minimal swelling of the parietal pleural mesothelium was seen with inflammatory infiltrates consisting of polymorphs and mononuclear cells. The visceral pleura showed some swelling of the mesothelial cells and, in the lungs, there were small subpleural and perivascular inflammatory infiltrates with polymorphs and mononuclear cells. On Day 8, a focal fibrotic reaction was noted in the parietal pleura with lymphocytes and polymorphs and swelling of the mesothelial lining cells. Swelling of cells was also seen in the visceral pleura. Intrapulmonary perivascular infiltrates with lymphocytes and histiocytes were also noted. At 42 days, a similar reaction to that on Day 8 was seen. The lymph nodes showed follicular lymphoid hyperplasia.

Physiological saline. On Days 1 and 8, slight infiltration and swelling of the mesothelial cells of the pleura was noted in some animals and there was slight perivascular intrapulmonary reaction with a few histiocytes and polymorphs. At the 42-day stage, except for slight infiltration of mesothelial lining of the pleura in one animal, no other abnormalities were seen.

Control group (anaesthetic only). Animals showed no abnormality on Day 1. Minimum perivascular infiltrates with eosinophils, histiocytes and lymphocytes were seen in one animal in the 8-day group and in two animals in the 42-day group. In these animals the lymph nodes were rather large and showed nodular hyperplasia.

Table I summarises the histological reaction of the various contrast agents and physiological saline control group on the pleura of rats. The χ^2 test for K independent samples showed a highly significant difference between the various contrast agents ($p < 0.001$). The Hytrast, Micropaque and pure barium sulphate groups produced a highly significant reaction ($p < 0.001$) compared with the combined control group (physiological saline and anaesthetic-only control groups were joined together to form one group as they were not significantly different from each other). There was a significant difference between the combined control group and Omnipaque ($p < 0.01$). There was no significant difference between Hexabrix, Gastrografin, Dionosil and the combined control group.

DISCUSSION

This study forms a part of the experimental work carried out to find a safe and suitable contrast agent for use in the gastrointestinal tract in cases where leakage may be suspected outside the lumen of the gut, particularly post-operatively. The contrast agent in such cases may leak into the mediastinum, pleura or peritoneum, or enter the lungs either by aspiration or direct fistula formation. Ideally, the contrast agent should not produce any toxic effect should it enter any of these regions. The conventionally used water-soluble contrast agent Gastrografin has been shown to be unsafe if it enters the lungs and may even cause death (Ansell, 1968; Chiu & Gambach, 1974). Experimentally, too, Gastrografin has been found to be unsafe in the lungs (Frech et al, 1970; Ginai et al, 1984).

The tissue reaction to various contrast agents has already been evaluated experimentally in the lung (Ginai et al, 1984), mediastinum (Ginai et al, 1985) and peritoneum (Ginai, 1985). The present study shows the tissue reaction of the various contrast agents on the pleura of rats.

Micropaque, pure barium sulphate and Hytrast produced highly significant reactions ($p < 0.001$) in the pleura of rats compared with the control groups. Pure barium sulphate and Micropaque were both visible radiographically (although somewhat less dense) in the thorax up to the 42nd day, whereas only very slight Hytrast rests were visible on the Day-42 radiographs. Dionosil, Hexabrix, Omnipaque and Gastrografin were no longer visible on the Day-1 radiographs and appeared to be completely absorbed in the first 24 h.

The factors which lead to the absorption of the contrast agent in the pleural space and the exact route of removal can only be postulated on the basis of literature studies. Another puzzling question concerns presence of contrast agent in the right pleural space when it was carefully injected into the left pleural space.

The mechanics of the pleural space have been extensively studied and reviewed by Agostoni (1972). "The absorption of liquid from the pleural cavity may occur through the lymphatics and the blood, that of particles and large molecules only through the lymphatics" (Dybkowsky, 1866, cited in Agostoni, 1972). Courtice and Simmonds (1954) reviewed the lymphatic drainage from the pleural cavity and concluded that nearly all absorption takes place in the parietal pleura. The communications between the lymphatics and pleural cavity do not seem to be permanent but occur due to temporary dehiscence of adjoining mesothelial cells occurring when the pleura is stretched. The importance of respiratory movement for passage of liquid and particles through the mesothelial lining and subserous tissues into the lymphatics and for the propulsion of the lymph stream is paramount. The lymphatics therefore appear to be an important route for drainage of pleural liquid, proteins and particles. Courtice and Simmonds (1949) studied the absorption of fluids from the pleural cavities of rabbits and cats, in particular, the absorption rate of 0.9% sodium chloride solution and of plasma injected into the pleural cavities of normal rabbits. According to those authors, anaesthetics slow down the absorption, but in unanaesthetised animals both saline and plasma are absorbed at about the same rate. When they injected 6 ml/kg of fluid, practically all was absorbed in 24 h. The rate of absorption was greatly increased by increasing respiratory movements. They also pointed out the differences between animal experiments and man. "In experimental animals the pleural investment is thin; the visceral layer is supplied by pulmonary artery. The mediastinum is mobile and material injected into one pleural cavity is almost invariably removed later from both sides." The results in the present experimental study would also confirm their point of view, as the contrast agent injected in the left pleural space was almost always seen in the right pleural space on the radiographs. The absorption of water-soluble contrast agents was fairly rapid, possibly only a few hours since, at 24 h, no sign of any pleural effusion or contrast agent was seen. The mobility of the mediastinum and a possible connection between the two pleural spaces must account, in the case of certain animals, for the presence of contrast agent in both pleural cavities.

Black (1972) also reviewed the pleural space and pleural fluid and found that the pleural space normally contains a very small amount of fluid and that the lymphatics are located in the subendothelial layer of the parietal pleura. Anteriorly, the parietal pleura drains into the internal mammary system, while posteriorly the pleura is drained into the intercostal lymph nodes. Eventually, lymph enters the vascular system through the right lymphatic trunk or the thoracic duct. The lymphatics of the visceral pleura drain into the mediastinal lymphatic system and then into the venous system by right lymphatic trunk or thoracic duct. Particulate matter (such as graphite and colloid iron), according to Courtice and Simmonds (1954), is absorbed mainly by the lower mediastinal pleura and costal parietal pleura in animals. Particulate matter is not absorbed by the visceral pleura. This fact is well demonstrated by the present experimental work, where pure barium sulphate and Micropaque were always found most abundantly in the inferior mediastinal pleura. The lower mediastinal pleura appears to the naked eye as a loose fatty tissue covered with pleural lining extending between the heart and diaphragm and anterior chest wall in the midline. The Micropaque series also showed filling of some of the mediastinal lymph nodes with contrast agent. This, however, was not found in the barium sulphate and Hytrast animals, which may be because not all of the mediastinal lymph nodes were included for histological section. It is also noteworthy that no absorption of the particulate contrast material is seen in the lungs and yet many lungs showed areas of patchy collapse and consolidation with all contrast agents. Although this may be due to intercurrent infection in some instances, the change is seen too frequently to be just a chance occurrence.

Another interesting observation is that the diaphragmatic lymphatics did not appear to fill with contrast agent. This is in contrast to the intraperitoneal injections (Ginai, 1985), where contrast agent filling of the diaphragmatic lymphatics and retrosternal lymphatics and lymph nodes was well defined in the case of pure barium sulphate, Micropaque and Hytrast. In the present series, no abdominal lymph nodes were seen to be filled with contrast agent. This difference in the peritoneal and pleural routes of absorption is also commented upon by Lemon and Higgins (1929). They point out the rarity with which pleural infections involve the peritoneum, whereas it is well known that pleural effusion may be associated with many abdominal pathological processes, such as Meig's syndrome, pancreatitis, peritoneal dialysis, and subphrenic abscess (Black, 1972).

In conclusion, the present study demonstrates that the water-soluble contrast agents Omnipaque, Gastrografin, Hexabrix and Dionosil cause the least reaction in the pleura, with Gastrografin and Hexabrix not being significantly different from the combined control group (saline/anaesthetic only). These two agents could be safely used, therefore, in cases where the possibility of leakage into the pleura may be suspected *e.g.* in the post-operative assessment of anastomotic upper gastrointestinal-tract surgery.

Previous experimental work on the lungs (Ginai et al, 1984) showed that Amipaque and Hexabrix were the least toxic contrast agents in the bronchi and lungs of rats, whereas Gastrografin caused significant reaction in these areas. Experimental work on the mediastinum (Ginai et al, 1985) demonstrated that Hexabrix and Gastrografin cause the least tissue reaction. Amipaque, Hexabrix and Gastrografin caused the least reaction in the peritoneum of rats (Ginai, 1985). In the light of these observations, it would appear that Gastrografin would not be suitable for use where there is risk of leakage directly into the lungs or aspiration into bronchi. This is because of a direct toxic effect on these tissues with the possibility of fatal reaction in patients if aspirated (Ansell, 1968; Chiu & Gambach, 1974). Amipaque is not ideal for practical use because of its high cost and its non-availability in a ready-to-use form.

In view of this, Hexabrix would be the contrast agent of choice in cases where leakage into the pleura, mediastinum or peritoneum may be suspected and aspiration may be an accompanying risk, and since starting its clinical use in our department, no untoward reactions have, so far, been recorded. A clinical study with Hexabrix is now being prepared.

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REFERENCES

AGOSTONI, E., 1972. Mechanics of the pleural space. *Physiological Reviews, 52,* 57.

ANSELL, G., 1968. A national survey of radiological complications: interim report. *Clinical Radiology, 19,* 175–191.

BLACK, L. F., 1972. The pleural space and pleural fluid. *Mayo Clinical Proceedings, 47,* 493–506.

CHIU, C. L. & GAMBACH, R. R., 1974. Hypaque pulmonary oedema—a case report. *Radiology, 111,* 91–92.

COURTICE, F. C. & SIMMONDS, W. J., 1949. Absorption of fluids from the pleural cavities of rabbits and cats. *Journal of Physiology, 109,* 117–130.

——1954. Physiological significance of lymph drainage of the serous cavities and lungs. *Physiological Reviews, 34,* 419–448.

FRECH, R. S., DAVIE, J. M., ADATEPE, M., FELDHAUS, R. & MCALISTER, W. H., 1970. Comparison of barium sulphate and oral 40% diatrizoate injected into the trachea of dogs. *Radiology, 95,* 299–303.

GINAI, A. Z., 1985. Experimental evaluation of various available contrast agents for use in the upper gastrointestinal tract in case of suspected leakage. Effects on peritoneum. *British Journal of Radiology, 58,* 969–978.

GINAI, A. Z., TEN KATE, F. J. W., TEN BERG, R. G. M. & HOORNSTRA, K., 1985. Experimental evaluation of various available contrast agents for use in the upper gastrointestinal tract in case of suspected leakage. Effects on mediastinum. *British Journal of Radiology, 58,* 585–592.

——1984. Experimental evaluation of various available contrast agents for use in the upper gastrointestinal tract in case of suspected leakage. Effects on lungs. *British Journal of Radiology, 57,* 895–901.

LEMON, W. S. & HIGGINS, G. M., 1929. Lymphatic absorption of particulate matter. *American Journal of Medical Science, 178,* 536–548.

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A model of semiautomatic type-specific diagnosis of brain tumours by computed tomography: mathematical fundaments and practical application

By *J. R. Iglesias, E. Kazner, †C. Aruffo and J. Esparza

Neurochirurgische Abteilung, Klinikum Charlottenburg, Freie Universität Berlin (Leiter Prof. Dr Ekkehard Kazner), Spandauer Damm 130, 1000 Berlin 19 and Institute of Neuropathology, Klinikum Steglitz, West Germany

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ABSTRACT

Applying Escudero's formula to Bayes' theorem of conditional probabilities, we have developed a mathematical model to diagnose type-specific brain tumours with great accuracy. We have transformed a multidimensional system of *n* characteristics on computed tomography into a linear system, making this model very easy to use and, thus, accessible to the clinician and radiologist. We tested this model in 177 brain tumours. In 86% of the cases we obtained a type-specific correct diagnosis, achieving better results than those previously reported. Suggestions are given as to how to improve this method further.

The use of computed tomography (CT) as a screening procedure on patients with mass-occupying processes in the brain has profoundly modified the overall neurosurgical diagnostic outlook and, hence, the therapeutic approach. However, accurate differential diagnosis of the different brain tumours by CT has not been easy up to now.

The use of a computer as an aid in making pre-operative diagnoses of organic brain lesions has been described (Du Boulay & Price, 1968; Kolber et al, 1974; Koller, 1976; Rioux & Nakache, 1979; Rotte, 1979; Wills et al, 1981,1982; Iglesias et al, 1985). Wills et al (1981,1982), using a discriminant analysis based on Bayes' theorem, obtained an accurate diagnosis of certain brain tumours by CT in 82.7% (either as a first, second or third choice) of the cases studied. It is the purpose of the present study to apply this methodology, using a personal computer, to obtain a mathematical model that will enable us to diagnose tumours from pre-operative CT scans with greater accuracy and objectivity.

MATERIAL AND METHODS

Three thousand seven hundred and fifty CT scans of patients with intracranial tumours from a previous German co-operative study (Kazner et al, 1981) were reviewed. In 3604 cases the diagnosis was verified histologically and tumours were classified according to the WHO norms. The neuropathologist made his diagnosis solely on the basis of the histological image; the appearance on CT in no way contributed to this diagnosis. We analysed the following types of intracranial tumours: astrocytomas, anaplastic astrocytomas, oligodendrogliomas, glioblastomas, pilocytic astrocytomas, ependymomas, medulloblastomas, lymphomas, plexus papillomas, meningiomas, and metastases. Both supra- and infratentorial tumours were included. The CT scans studied were divided into two groups according to the age of the patients (older and younger than 15 years) because the localisation and incidence of brain tumours are not always the same in these age groups.

The following characteristics on CT were collected for each tumour in both age groups and were used to evaluate the CT: predominant localisation (frontal, parietal, temporal, occipital, midline, brain stem, sellar, intraventricular, cerebellar, or cerebello-pontine angle), X-ray absorption (hypo- and hyperdensity), enhancement after injection of contrast material, perifocal oedema, calcifications, post-contrast ring enhancement, lesion delimitation and multiplicity of the lesion. We considered as hypodense those tumours which appeared darker than the normal brain tissue, that is, where the absorption was reduced. Hyperdense tumours were those which appeared lighter than the cerebral tissue because of an increased absorption. The degree of hypo- and hyperdensity was not considered. Under oedema we did not consider any grading (Kazner et al, 1981), but just considered the presence or absence of oedema, regardless of the degree. These characteristics were entered into the computer. The diagnosis obtained in this manner was then compared with the histological diagnosis.

The CT scans of the 3750 patients were used as a data base ("training field") and 177 new CT scans, for each of which the patient had a confirmed histological diagnosis, were used as a "test field" to evaluate our method. A personal computer Commodore/8032 (32 KB RAM) with a dual-drive floppy disk (8050) was used. The programming language used was Commodore's Microsoft Basic.

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* Author for correspondence.

† On leave from the Institute of Biomedical Research, UNAM, Mexico with a DAAD fellowship.

TABLE I

PROBABILITIES *A PRIORI* OF THE TUMOURS STUDIED

Type of neoplasm	Probability *a priori*	
	older than 15 years	younger than 15 years
Astrocytoma	0.085	0.199
Anaplastic astrocytoma	0.070	0.020
Oligodendroglioma	0.058	0.060
Glioblastoma	0.190	0.060
Pilocytic astrocytoma	0.056	0.180
Ependymoma	0.056	0.098
Medulloblastoma	0.045	0.180
Lymphoma	0.044	0.001
Plexus papilloma	0.031	0.141
Meningioma	0.215	0.060
Metastasis	0.150	0.001

RESULTS

Mathematical foundations

According to Bayes' theory of decision, the interpretation of a test result or of any other finding rests equally upon two factors: probability *a priori* and conditional probability.

The values of the probability *a priori* of each diagnosis, in both age groups, was calculated (Table I) by obtaining the mean of probabilities for each group, as described in the literature (Jänisch et al, 1980; Kazner et al, 1981; Wills et al, 1981; Jellinger & Machacek, 1982; Schreiber et al, 1982; Wills et al, 1982; Iglesias et al, 1983).

To calculate the conditional probability, the distribution of the different characteristics on CT must be taken into account. This probability was calculated independently in the two age groups considered (Tables II, III). We have assumed that the characteristics on CT follow, as seen histologically (Iglesias et al, 1983), a binomial distribution. In a binomial distribution the best estimation for a tumour of the "training field" to belong to a given diagnosis is the relative frequency of each characteristic in each diagnosis (Escudero, 1977; Iglesias et al, 1983).

Practical application

The discriminant function is obtained by transforming the product of the probability *a priori* and the conditional probability into a linear function.

A tumour is given a determined diagnosis, D_i, if its discriminant function $G_i(S_j)$ has a maximal value among one of the n given diagnoses (in this series $n = 11$) To establish the maximal discriminant function and its corresponding probability, the following steps have to be taken using a computer.

(1) Calculation of the values of the n discriminant functions in a given CT scan and their arrangement in descending rank; (2) calculation of the differences between the n discriminant functions which gives $n-1$ values; (3) calculation of the mean of the differences; (4) if the first difference is greater than the mean, then the tumour belongs to the first diagnosis because the difference between the first and second discriminant functions is greater than the mean and has, thus, a maximal probability. If the first difference is smaller than the mean, then the tumour belongs to the first and second diagnoses because it can not differentiate one from the other, and so on. Its exact probability *a posteriori* $P(D_i/S_j)$ must be calculated with the following formula:

$$P(D_i/S_j) = \frac{\exp G_i(S_j)}{\sum \exp G_i(S_j)}$$

where $G_i(S_j) = AV_0 + AV_i S_k$ (AV_0 = influence of the class; AV_i = influence of the characteristics S_k). Thus, the computer displays and outputs values of diagnoses in descending rank of probabilities, with a limit of 0.01 to avoid having a long list of differential diagnoses which are of little value, as seen in the following examples.

Tumour 8	Histological diag.:	lymphoma	
	Computer CT diag.:	lymphoma	53.26%
		anaplastic astrocytoma	39.47%
Tumour 25	Histological diag.:	plexus papilloma	
	Computer CT diag.:	ependymoma	59.37%
		plexus papilloma	36.15%
Tumour 159	Histological diag.:	astrocytoma	
	Computer CT diag.:	astrocytoma	64.04%
		anaplastic astrocytoma	24.30%
		oligodendroglioma	8.39%
		lymphoma	1.90%
		pilocytic astrocytoma	1.11%

When we applied this mathematical model to the 177 cases of our "test field" and then compared the diagnosis by CT with the histologically confirmed diagnosis, 86% were type-specifically correctly diagnosed (Table IV).

DISCUSSION

Bayes' theorem has been used to classify clinically radiologically different intracerebral processes with a percentage of correct diagnoses which oscillates between 69% and 88% when considering the first, second and third choices as being correct (Rotte, 1979; Wills et al, 1981,1982). However, because these previous works have not dealt with the same groups of tumours we studied, it is difficult to make any comparisons as to the degree of success. Applying Escudero's formula (Escudero, 1977), which is based on the analysis of the distribution of given characteristics, it was possible to obtain an histologically correct diagnosis of brain tumours in 92.77% (Iglesias et al, 1983) of the cases studied and a cytologically correct diagnosis of thyroid tumours was obtained in 91% (Scholman et al, 1984). In

TABLE II

FREQUENCY/100 OF CHARACTERISTICS ON CT IN CHILDREN

Diagnosis	1 Frontal	2 Parietal	3 Temporal	4 Occipital	5 Midline	6 Brain stem	7 Perisellar	8 Ventricular	9 Cerebellar	10 CPA	11 Hypodensity	12 Hyperdensity	13 Contrast +	14 Perifocal oedema	15 Calcification	16 Ring enhancement	17 Clear delimitation	18 Multiplicity
Astrocytoma	0.12	0 12	0.12	0.11	0.05	0.36	0.08	0.00	0.04	0.00	0.980	0.000	0.020	0.019	0.170	0.200	0.200	0.001
Anaplastic astrocytoma	0.19	0.10	0.19	0.18	0.06	0.18	0.00	0.00	0.01	0.00	0.330	0.190	0.745	0.675	0.150	0.700	0 500	0 015
Oligodendroglioma	0.24	0.25	0.24	0.24	0.00	0.00	0.01	0.00	0.01	0 00	0.258	0.137	0.430	0.379	0.700	0.200	0.200	0 001
Glioblastoma	0.14	0.10	0.14	0.14	0.08	0.28	0.00	0.00	0.08	0.00	0.090	0 085	0.940	0.917	0.100	0.990	0 950	0.002
Pilocytic astrocytoma	0.01	0.01	0.01	0.01	0.166	0.25	0.00	0.00	0.523	0.02	0.312	0.150	0.776	0.250	0.000	0.000	0.000	0.001
Ependymoma	0.00	0.00	0.00	0.00	0.00	0 01	0.00	0.96	0.03	0.00	0.129	0.407	0.750	0.425	0.250	0.000	0.950	0 001
Medulloblastoma	0.00	0.00	0.00	0.00	0.00	0.01	0.00	0.00	0.99	0.00	0.044	0.641	0.830	0.462	0.160	0.000	0.500	0.001
Lymphoma	0.30	0.30	0.30	0.10	0.00	0 00	0.00	0.00	0.00	0.00	0.145	0 435	0.870	0.725	0 000	0.000	0.000	0.025
Plexus papilloma	0 00	0.00	0.00	0.00	0.00	0.02	0.00	0.97	0.00	0.01	0.000	0.640	0.928	0.428	0.100	0.000	0.999	0 001
Meningioma	0.19	0.19	0.18	0.18	0.18	0.08	0.00	0.00	0.00	0.00	0.008	0.732	0 882	0 612	0.700	0 000	0.999	0.002
Metastasis	0.00	0.00	0.00	0.00	0.00	0 00	0.00	0.00	0.00	0.00	0.168	0.337	0.886	0.869	0.070	0.990	0.500	0.456

CPA = cerebello-pontine angle.

TABLE III

FREQUENCY/100 OF CHARACTERISTICS ON CT IN ADULTS

Diagnosis	1 Frontal	2 Parietal	3 Temporal	4 Occipital	5 Midline	6 Brain stem	7 Peri-sellar	8 Ventricular	9 Cerebellar	10 CPA	11 Hypo-density	12 Hyper-density	13 Contrast +	14 Peri-focal oedema	15 Calcification	16 Ring enhancement	17 Clear delimitation	18 Multiplicity
Astrocytoma	0.33	0.20	0.34	0.05	0.01	0.03	0.01	0.01	0.02	0.00	0.980	0.000	0.020	0.019	0.170	0.200	0.200	0.001
Anaplastic astrocytoma	0.24	0.23	0.38	0.09	0.03	0.01	0.00	0.01	0.01	0.00	0.330	0.190	0.745	0.675	0.150	0.700	0.500	0.015
Oligodendro-glioma	0.35	0.23	0.27	0.07	0.05	0.00	0.00	0.03	0.00	0.00	0.258	0.137	0.430	0.379	0.700	0.200	0.200	0.001
Glioblastoma	0.16	0.27	0.42	0.13	0.00	0.01	0.00	0.00	0.01	0.00	0.090	0.085	0.940	0.917	0.100	0.990	0.950	0.002
Pilocytic astrocytoma	0.01	0.01	0.02	0.02	0.04	0.20	0.00	0.00	0.70	0.01	0.312	0.150	0.776	0.250	0.000	0.000	0.000	0.001
Ependymoma	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.90	0.02	0.08	0.129	0.407	0.750	0.425	0.250	0.000	0.950	0.001
Medullo-blastoma	0.01	0.00	0.00	0.00	0.00	0.10	0.00	0.01	0.85	0.03	0.044	0.641	0.830	0.462	0.160	0.000	0.500	0.001
Lymphoma	0.20	0.20	0.10	0.10	0.08	0.10	0.00	0.20	0.02	0.00	0.145	0.435	0.870	0.725	0.000	0.000	0.000	0.025
Plexus papilloma	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.90	0.09	0.01	0.000	0.640	0.928	0.428	0.100	0.000	0.999	0.001
Meningioma	0.15	0.06	0.09	0.03	0.48	0.01	0.12	0.01	0.01	0.06	0.008	0.732	0.882	0.612	0.700	0.000	0.999	0.002
Metastasis	0.30	0.16	0.10	0.16	0.03	0.04	0.01	0.01	0.19	0.00	0.168	0.337	0.886	0.869	0.070	0.990	0.500	0.456

CPA = cerebello-pontine angle.

TABLE IV

MATHEMATICAL CLASSIFICATION OF BRAIN TUMOURS BY CT

Diagnosis by CT	Correct diagnosis	Incorrect diagnosis	Total
Astrocytoma	11 (100%)	0	11
Anaplastic astrocytoma	15 (88.2%)	2 (11.8%)	17
Oligodendroglioma	6 (66.7%)	3 (33.3%)	9
Glioblastoma	25 (92.6%)	2 (7.4%)	27
Pilocytic astrocytoma	18 (94.7%)	1 (5.3%)	19
Ependymoma	13 (100%)	0	13
Medulloblastoma	14 (87.5%)	2 (12.5%)	16
Lymphoma	7 (70.0%)	3 (30.0%)	10
Plexus papilloma	0	6 (100%)	6
Meningioma	31 (91.2%)	3 (8.8%)	34
Metastatis	12 (80.0%)	3 (20.0%)	15
Totals	152 (85.9%)	25 (14.1%)	177

this study we have obtained a correct first-choice diagnosis by CT using Escudero's formula in 86% of the CT scans analysed.

The success in discriminating among certain tumours, for example, astrocytomas and anaplastic astrocytomas, in which in some instances it may seem the divisions are indecisive, was obtained by taking into account those characteristics which clearly differentiate one tumour type from the other. In this example the decisive characteristics, as seen in Table II and III, were: hypodensity (in 98% of astrocytomas but only 33% of the anaplastic astrocytomas), hyperdensity (0% in astrocytomas in comparison with 19% in anaplastic astrocytomas), and the enhancement after contrast material (in only 2% of the astrocytomas but in 75% of the anaplastic astrocytomas). These differences related to the malignancy of a tumour could be correlated very well with their histopathological image. The same approach has also been successfully used by other authors (Wills et al, 1981,1982).

One of the factors which lead to errors in the diagnosis was that the morphology of some tumours, as depicted by the CT scan, showed a very similar pattern. Such is the case for ependymomas and plexus papillomas, as previously described by other authors (Kazner et al, 1978, 1981). In order to discriminate one diagnosis from another it is important for all tumours of the same histological type to have similar characteristics on CT and that these be sufficiently different from those seen in other tumours. Because this was not the case for ependymomas and plexus papillomas we can say that the cases wrongly diagnosed were due to the tumoral characteristics considered and not to the mathematical model used. It must be said, however, that the diagnosis of plexus papilloma was not totally excluded but was always given as a second choice in the list of differential diagnosis with a little difference in probabilities as compared with the ependymomas. Considering the first and second choices as correct diagnoses the cases correctly diagnosed would be considerably higher than 86%.

In order to improve our results more characteristics, such as degree and localisation of oedema, lesion contour and so on, should be included. The interaction of these characteristics, as given by this mathematical model, would permit a more precise discrimination and, therefore, a more exact diagnosis. In fact, we believe that our errors in the diagnosis of plexus papillomas occurred because we did not take into account the contour of the lesion. However, it is interesting to notice that although we considered relatively few characteristics on CT, the degree of correctly diagnosed cases was relatively high, although no comparisons may be made with the results of other authors using the same methodology (Ambrose et al, 1975; Collard & Dupont, 1978; Wills et al, 1981, 1982) because we have considered a more restricted set of diseases and so comparisons could be misleading. The high accuracy of this system permits the confirmation of a diagnosis with CT, although a final histological confirmation is always desirable.

This method gives more precise and objective CT diagnoses and reduces the degree of human error, since the comparison of every CT problem with previously established, discriminant functions for each diagnosis reduces subjectivity. At the same time it provides an updated archive which allows the rapid location of similar or identical cases, thus facilitating a clinical-CT-histological correlation, and is easy to use (Teather et al, 1985; Wills et al, 1981, 1982).

The computer provides, at the same time, differential diagnoses expressed in percentages of probabilities *a posteriori*. This is easily achieved by transforming a multidimensional system of $n \times m$ dimensions (n characteristics in m diagnoses) into a linear system $G_i(S_j)$.

This model lightens the diagnostic decision of the physician and allows an easy and objective learning of the characteristics which determine each category. Very important is the fact that this method requires only a simple computer, is very rapid and is programmed in BASIC, all of which makes it accessible. Although this semiautomatic method facilitates the physician's work, it does not diminish the importance of his decision-making (Teather et al, 1985).

REFERENCES

AMBROSE, J., GOODING, M.R. & RICHARDSON, A. E., 1975. Sodium iothalamate as an aid in the diagnosis of intracranial lesions by computerized transversal axial scanning. *Lancet, ii*, 669–674.

COLLARD, M. & DUPONT, H., 1978. Critical of the errors in brain tomodensitometry. In *The Diagnostic Limitations of Computerized Axial Tomography*. Ed. by J. Bories (Springer-Verlag, Berlin), pp. 178–189.

DU BOULAY, G. H. & PRICE, V. E., 1968. The diagnosis of intracranial tumours assisted by computer. *British Journal of Radiology, 41*, 762–781.

ESCUDERO, L. F., 1977. *Reconocimiento de Patrones.* (Paraninfo, Madrid), pp. 1–688.

IGLESIAS, J. R., SANCHEZ, M.J., SANDRA, A. & MOHNHAUPT, A., 1983. Computer model of archive and diagnosis of brain tumours based on the WHO classification. *EDV für Medizin und Biologie, 14*, 40–44.

IGLESIAS, J. R., KAZNER, E., ARUFFO, C. & ESPARZA, J., 1985. CT diagnosis of brain tumours: semiautomatic type-specific diagnosis with the help of a personal computer Mathematical fundaments and practical application In *Computerized Assisted Radiology* Ed. by H. U. Lemke, M. L. Rhodes, C C. Jaffee & R Felix (Springer-Verlag, Berlin), pp. 443–448.

JÄNISCH, W., SCHREIBER, D. & GERLACH, H., 1980. *Tumoren des Zentralnervensystems bei Feten und Säuglingen.* (VEB Gustav Fischer Verlag, Jena), pp. 1–555.

JELLINGER, B. & MACHACEK, E., 1982. Rare intracranial tumours in infancy and childhood. In *Tumours of the Central Nervous System in Infancy and Childhood.* Ed. by D. Vogt, P. Gutjahr & C. Langmaid (Springer-Verlag, Berlin), pp. 44–52

KAZNER, E., WENDE, S., GRUMME, TH., LANKSCH, W. & STOCHDORPH, O., 1981. *Computertomographie Intrakranieller Tumoren aus Klinischer Sicht.* (Springer-Verlag, Berlin), pp. 1–548.

KAZNER, E., WILSKE, J , STEINHOFF, H. & STOCHDORPH, O., 1978. Computer assisted tomography in primary malignant lymphomas of the brain. *Journal of Computer Assisted Tomography, 2*, 125–134.

KOLBER, T., VIRNICH, H. & WINCKLER, C., 1974. Präoperative Artdiagnostik hirnorganischer Prozesse mit hilfe eines Computerprogramms. *Acta Neurochirurgica, 31*, 23–28.

KOLLER, S., 1976. Mathematisch-statistische Grundlagen der Diagnostik. *Klinischen Wochenschrift, 45*, 1065–1072.

RIOUX, P. & NAKACHE, J. P , 1979. Discriminant analysis: methods and program. *Computer Programs in Biomedicine, 10*, 43–47.

ROTTE, H. E., 1979. Zur Anwendung der computergestützten Röntgendiagnostik in der Onkologie *Archiv für Geschwulstforschung, 49*, 347–356.

SCHOLMAN, H. J., PFANKUCH, F., IGLESIAS, J. & BRINNEL, CH., 1984. Microcomputer als Hilfsmittel in der zytologischen Diagnostik bei Erstellung von Befundberichten. *Verhandlung der Deutsche Gesellschaft für Pathologie, 68*, 428.

SCHREIBER, D., JÄNISCH, W. & GERLACH, H., 1982. Tumours in infancy, childhood and adolescence. In *Tumours of the Central Nervous System in Infancy and Childhood.* Ed. by D. Vogt, P Gutjahr & C. Langmaid (Springer-Verlag, Berlin), pp. 62–68.

TEATHER, D., MORTON, B. A., DU BOULAY, G. H., WILLS, K. M., PLUMMER, D. & INNOCENT, P. R., 1985. Computer assistance for CT scan interpretation and cerebral disease diagnosis. *Statistics in Medicine, 4*, 311–315.

WILLS, K., DU BOULAY, G. H. & TEATHER, B., 1981. Initial findings in the computer-aided diagnosis of cerebral tumours using CT scan results. *British Journal of Radiology, 54*, 948–952.

WILLS, K , TEATHER, D & DU BOULAY, G. H., 1982. An improvement in computer-aided diagnosis of meningiomas after CT. *Neuroradiology, 22*, 255–257.

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Nuclear cardiology: a comparison of equilibrium gated blood pool and gamma camera first-pass measurements for the assessment of left-ventricular regional wall motion

By D. N. Taylor, Ph.D., S. Choraria, M.R.C.P., *J. Mills, B.Sc., J. Flint, M.R.C.P., J. A. McIntosh, B.Sc. and J. Pilcher, F.R.C.P.

Departments of Medical Physics and Cardiology, Walsgrave Hospital, Coventry

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ABSTRACT

There are two major problems remaining for the successful assessment of left-ventricular regional wall motion (RWM) using nuclear cardiology. These are as follows. Which technique should be used: first pass or equilibrium? Secondly, which views should be used to give full information about the RWM of the left ventricle? This paper specifically considers each of these questions and concludes that equilibrium blood pool imaging in both the right anterior oblique and left anterior oblique projections is currently the best option.

There are now two established nuclear cardiology techniques for the assessment of left-ventricular (LV) function. Multiple-gated equilibrium studies have been used with conventional gamma cameras since the late '70s (Folland et al, 1977). To calculate left-ventricular ejection fraction (LVEF) and to visualise regional wall motion (RWM) in the antero-septal and postero-lateral segments of the left ventricle, the left anterior oblique (LAO) 45° viewing direction is used, which gives clear separation of the ventricles. To visualise RWM in antero-lateral and postero-septal segments of the left ventricle there is no viewing direction which gives a clear view of the LV segments. Various viewing directions have been proposed. These include the anterior view (Pichler, 1978), the right anterior oblique (RAO) view (Harris et al, 1981), the left lateral view (Kelly et al, 1981) and the left posterior oblique (LPO) view (Winzelberg, 1980). Logistics dictate that some choice must be made to determine the correct complementary view to the LAO view.

The other radionuclide technique is to use the first passage of radionuclide through the heart and, thus, temporally separate the cardiac chambers. This has worked extremely well with the high count-rate capability multicrystal device, the autofluoroscope (Dymond et al, 1979), and has been proposed for the conventional gamma camera (Pachinger et al, 1979). However, the technique has not found widespread acceptance and the probable reasons for this lie in the limited count-rate capability of conventional gamma cameras (Taylor, 1981). With the advent of high count-rate capability gamma cameras, the first-pass methods should prove more useful, but to date no published series exist for the evaluation of LV RWM using this technique with modern gamma cameras.

In the present study, RWM assessment from high count-rate first-pass and multiview equilibrium studies have been validated against X-ray ventriculography.

PATIENTS AND METHODS

Twenty-one unselected patients who had undergone contrast ventriculography for the assessment of ischaemic heart disease (18), valvular disease (three), or heart failure (13) were investigated by radionuclide ventriculography within 5 days of catheterisation. The 21 patients represented a full range of cardiac function, from an LVEF of 16% with high RWM abnormality score to an LVEF of 62% with only minor RWM abnormality score. Only one patient had an entirely normal left ventricle on X-ray ventriculography. Each patient had a 30° RAO first-pass study followed by equilibrium blood pool imaging in the LAO, RAO and LPO projections.

Single-plane (30° RAO) contrast ventriculography was performed using standard methods. The resulting angiograms were visually assessed by two experienced observers. The left ventricle was divided into five segments and RWM visually assessed for each segment. In the RAO view the five segments of the left ventricle were proximal antero-lateral, distal antero-lateral, apical, distal diaphragmatic and proximal diaphragmatic. A five-point movement scale was used for visual assessment of RWM: 0, normal movement; 1, mild hypokinesis; 2, marked hypokinesis; 3, akinesis; 4, dyskinesis.

Radionuclide first-pass studies were done in the 30° RAO projection. The gamma camera used was the Elscint Apex. The 10% loss count rate was measured at 40 kcounts/s and the maximum count rate at 75 kcounts/s, with scatter. The count rates obtained during LV passage were around 50 kcounts/s from an injected dose of 700 MBq of $^{99}Tc^{m}$ in the form of pertechnetate. No special bolus technique was used but the bolus quantity was checked and was comparable with published data (Lane et al, 1971). The FWHM of the injection bolus at superior vena cava passage was 3.9 ± 1.5 s.

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*Now at Department of Medical Physics, Clatterbridge Hospital, Liverpool.

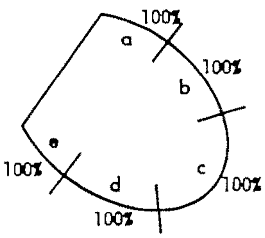

FIG. 1.

Interobserver variability. X-ray contrast ventriculography. Percentage agreement within one grade of motion between two observers. Segments (in this and following figures) (a) proximal antero-lateral, (b) distal antero-lateral, (c) apex, (d) distal diaphragmatic, (e) proximal diaphragmatic.

Equilibrium gated blood pool acquisitions were done in the 30° RAO, 45° LAO (modified) and 45° LPO projections. Data were acquired for 24 frames per heart cycle, and not less than 20 000 counts total in the left ventricle per frame were acquired. Typically, the acquisition took 6–10 min. Prior to visual assessment the data were smoothed up to twice using a standard binomial nine-point filter.

The radionuclide results for the RAO and LPO projections were assessed by two experienced observers using the same five regions of the LV and the same five-point scale of motion as the contrast ventriculograms. Cine display of the real-time heart cycles was used at the visual assessment. For all assessments the patient data were presented to the observers in a randomised way so that they had no knowledge of the patient details.

RESULTS

The interobserver variability for X-ray contrast ventriculograms was obtained from the two independent observers' results. For each of five segments in 21 patients the observers' scores were compared. Agreement to within less than or equal to one unit on the five-point motion scale was chosen as an acceptable level of agreement. In all segments of the left ventricle in all patients there was agreement to within one point between the observers. This is shown diagrammatically in Fig. 1.

The interobserver variability for radionuclide first passage was evaluated for the same five LV segments in the 30° RAO view. For two patients out of the 21 the acquisition of the first-pass data failed and no reasonable results were obtained. The two observers' scores were again compared and the percentage which agreed to within less than or equal to one on the five-point motion scale was calculated. These are shown in Fig. 2.

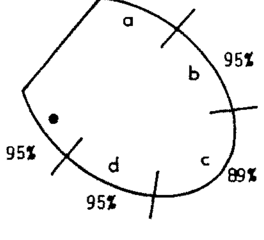

FIG 2.

Interobserver variability: radionuclide first-pass. Percentage agreement within one grade of motion between two observers.

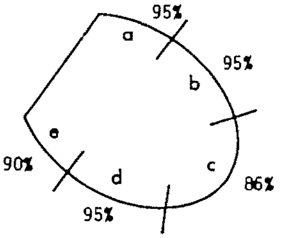

FIG. 3.

Interobserver variability: radionuclide equilibrium RAO. Percentage agreement within one grade of motion between two observers.

Interobserver variability for equilibrium gated blood pool acquisitions in the RAO view are shown in Fig. 3 and for the LPO view in Fig. 4.

Another index of interobserver variation is obtained by calculating the mean difference per segment between the observers on the scale of zero to four A mean value of zero would indicate no difference; a mean value of four would indicate very discrepant assessment between the two observers. The mean value of the observer difference per segment was 0.25 for the X-ray contrast ventriculography, 0.47 for radionuclide first pass, 0.51 for radionuclide equilibrium RAO and 0.67 for the radionuclide equilibrium LPO view.

The results of the RWM assessment for each of the five segments by each method are given in Table I. The mean of the two observers is used for the RWM score for any particular segment.

For each of the radionuclide studies the difference between the RWM score and the RWM score for X-ray contrast ventriculography was assessed. Firstly, the percentage of segments where the scores were agreed to less than or equal to one unit (on a five-point scale) was assessed. Secondly, the mean difference per segment between the observers was calculated. (This was the same analysis as was done for interobserver variability.)

For first-pass radionuclide studies the percentage of similar RWM scores for each segment is seen in Fig. 5. The highest agreement is seen in the proximal antero-lateral segment, where in 79% of cases (15 out of 19) there is not more than one unit difference between first-pass radionuclide and X-ray contrast ventriculography. The worst agreement is seen at the apex, where only in 53% of cases (10 out of 19) is there similarity of RWM score. This level of agreement is far poorer than the interobserver variabilities for either X-ray contrast ventriculography or radionuclide first pass.

The mean difference per segment between X-ray contrast ventriculography and radionuclide first-pass scores was 0.82, averaged over all five segments.

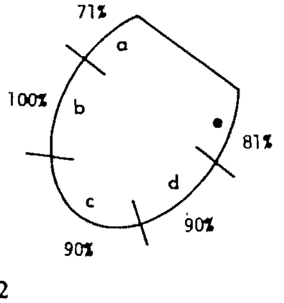

FIG. 4.

Interobserver variability: radionuclide equilibrium LPO. Percentage agreement within one grade of motion between two observers.

For radionuclide equilibrium studies in the RAO 30° view, the percentage of similar RWM scores for each segment is seen in Fig. 6. The highest agreement is seen in the proximal antero-lateral and apical segments, where 95% (20 out of 21) of cases show similar RWM scores. The worst agreement is in the proximal diaphragmatic segment, where 81% (17 out of 21) of cases show similar RWM scores. This level of agreement between the two techniques is similar to the interobserver variation for the techniques.

The mean difference per segment between X-ray contrast ventriculography and radionuclide equilibrium RAO scores was 0.56, averaged over all five segments.

For radionuclide equilibrium studies in the LPO view the percentage of similar RWM scores for each segment is seen in Fig. 7. The highest agreement is seen in the distal diaphragmatic segment, where 90% (19 out of 21) of cases show similar RWM scores. The poorest

TABLE I

Regional wall motion scores for each of five segments of the left ventricle for four methods

Case	Method*	Region				
		(a)	(b)	(c)	(d)	(e)
1	X	0	1	2	1	0
	FP	2	3	3.5	3	3
	ER	0	2.5	2.5	1.5	0
	EL	2	2	3.5	2	1.5
2	X	0	0	1	2	2
	FP	1.5	2.5	4	2.5	2
	ER	0.5	1.5	1	1	0
	EL	0.5	0.5	0	2	1
3	X	0	1.5	2	2	1.5
	FP	0.5	1.0	1.5	0.5	1.0
	ER	0	2.5	3	1	0
	EL	0.5	2	3	1.5	1
4	X	0	0	0.5	0	0
	FP	0	0	0	0.5	1.5
	ER	0	0	0	0	0
	EL	1	0.5	0.5	0.5	1.5
5	X	0	1	1.5	2	1
	FP	0	0	0	1	1.5
	ER	0	1	2	1.5	0
	EL	0	0.5	1	1.5	0.5
6	X	0	0	1.5	2.5	2
	FP	1.5	1.5	1	2.5	2.5
	ER	0	0	0.5	1.0	0.5
	EL	2.5	1.5	1	2	1
7	X	0	1.5	3.5	2	0
	FP					
	ER	0.5	1.5	3.0	0.5	0
	EL	1	1	3	1.5	0.5
8	X	0	1.5	0	1.5	2.5
	FP					
	ER	0	1	1	2.5	2.0
	EL	3	3	2	1.5	2.5
9	X	1.5	1	2	2.5	2.5
	FP	1.5	2	3.5	1.5	1.5
	ER	0.5	2	2	1.5	1.5
	EL	1	1	1.5	2	2
10	X	0	2	4	1.5	0
	FP	0	1	2	1	0
	ER	0	1.5	3	1	0
	EL	0	0	0.5	0	0
11	X	1	1.5	2	3	2
	FP	0	0	0.5	1.5	1
	ER	0	1	2	2	1
	EL	0	0.5	1.5	2.5	1.5
12	X	0	0.5	0	0	0.5
	FP	0	0	0	0	0.5
	ER	0	0	0	0	0.5
	EL	1	0	0	1	1.5
13	X	0	0	0.5	0.5	0
	FP	0	0	0	0	0
	ER	0	0.5	0	0	0
	EL	0	0	0	0	0
14	X	1.5	1	1	3	2.5
	FP	0	1	3	1.5	1
	ER	1.5	2	2.5	1.5	1.5
	EL	1	1.5	2	2.5	3
15	X	0	1	2	2	0
	FP	0	0	0.5	1	0
	ER	0	1.5	2.5	1.5	1
	EL	1.5	1.5	1.5	0.5	0.5
16	X	0	1	1.5	1	0
	FP	0.5	2	1.5	1.5	1.5
	ER	0	1.5	1.5	1.5	0.5
	EL	0	1	0	1	0.5
17	X	0	0	1	0	1.5
	FP	0	0	0	0	0
	ER	0	0	0	0	0
	EL	0.5	0	0	0	0
18	X	0	0	0	0	0
	FP	0	0	0	0	0
	ER	0	0.5	1.0	0.5	0
	EL	0	0	0	0	0
19	X	0	0	1	0	1.5
	FP	0	0.5	1	2	1.5
	ER	1.5	1.5	2	1	0.5
	EL	0	0.5	1.5	0	0
20	X	0	0	0	0.5	2
	FP	0.5	2	2	2	1
	ER	0	0.5	0	0	1
	EL	1	1.5	0.5	0.5	1
21	X	0	1.5	1	1	0
	FP	0.5	0.5	0	1	1.5
	ER	0	0.5	1	1	0.5
	EL	1.5	0	0.5	0	1

*X = X-ray contrast ventriculography, FP = first-pass radionuclide, ER = equilibrium gated RAO view, EL = equilibrium gated LPO view.

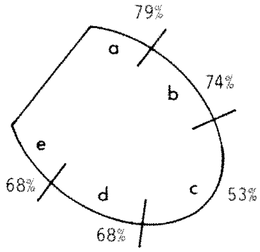

Fig. 5.

Agreement between radionuclide first-pass and X-ray contrast ventriculography. Percentage agreement within one grade of motion between two techniques.

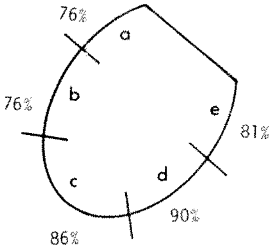

Fig. 7.

Agreement between radionuclide equilibrium LPO and X-ray contrast ventriculography. Percentage agreement within one grade of motion between two techniques.

agreement is seen in both the proximal and distal antero-lateral segments, where 76% (16 out of 21) of cases show similar RWM scores. This level of agreement is worse than the interobserver variability for either technique.

The mean difference per segment between X-ray contrast ventriculography and radionuclide equilibrium LPO scores was 0.72, averaged over all five segments.

Discussion

We have used visual assessment of X-ray contrast ventriculograms as the gold standard against which the radionuclide RWM was assessed. This is because this technique represents the currently accepted method of choice in cardiology. Certainly, we found that it has a low interobserver variability (Fig. 1). Also, between two independent observers the mean difference in RWM score averaged over the five segments was 0.25 (Table II). With a five-point motion scale used to assess RWM, this average difference of 0.25 of one unit represents very good agreement between the two observers.

The choice of radionuclide technique has previously been equilibrium gated blood pool, since the count rates obtained during first passage have exceeded the capabilities of conventional gamma cameras. With the advent of high count-rate performance gamma cameras, first-pass studies appear most attractive for the complementary view to the equilibrium LAO view. We have shown that the interobserver variability of the first-pass studies is acceptable, with two observers finding similar RWM scores in about 95% of cases. (The variability is slightly better at the proximal antero-lateral wall and slightly worse at the apex.) However, the agreement between radionuclide first-pass and X-ray contrast ventriculography RWM scores is not good (Fig. 5), agreement occurring in only about 68% of cases (varying from 79% at the proximal antero-lateral segment to 53% at the apex). This is also seen in the average difference score per segment of 0.82 averaged over the five segments. This is considerably higher than the mean interobserver variabilities of 0.25 per segment for X-ray contrast ventriculography or 0.47 for radionuclide first pass (Table II).

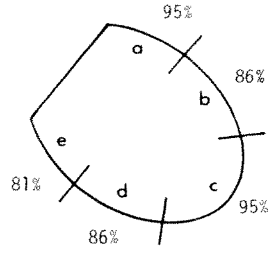

Fig. 6.

Agreement between radionuclide equilibrium RAO and X-ray contrast ventriculography. Percentage agreement within one grade of motion between two techniques.

Equilibrium gated blood pool studies have previously been used for assessment of RWM in the left ventricle. Many authors have used the RAO 30° view to complement the LAO 45° view (Brady et al, 1979; Harris et al, 1981). Our findings would confirm this. We used a 30° RAO projection from a slant-hole collimator placed adjacent to the chest wall. A consideration of imaging geometry would support the view that there would be little difference between the anterior view and a 30° RAO view. A small advantage for the 30° RAO view is that it is more nearly orthogonal to the LAO 45° view. The interobserver variability for the equilibrium RAO view is good, with two observers finding similar RWM scores in about 92% of cases (varying from 95% to 80% depending on the LV segment considered). The agreement with X-ray contrast ventriculography is good, the two techniques giving similar RWM scores in about 89% of cases (varying from 95% at the proximal antero-lateral and apical segments to 81% in the proximal diaphragmatic segment). This is very similar to the interobserver figures and shows high accuracy for RWM assessment with the equilibrium RAO 30° view. The mean difference per segment in the RWM scores from the two techniques is 0.56, which, again, is not significantly different from the interobserver variation for the techniques. We have used a level of agreement of less than or equal to one point on a five-point scale. It is interesting to note that if the agreement criterion is made more demanding (*i.e.* exact agreement in the RWM score from the two techniques) the present findings are very similar to those of Harris et al (1981).

TABLE II

Interobserver and intermethod differences: mean difference per segment

	Interobserver difference	Intermethod difference
X-ray ventriculography	0.25	—
Nuclear first pass	0.47	0.82
Nuclear equilibrium RAO	0.51	0.56
Nuclear equilibrium LPO	0.67	0.72

They showed exact agreement in RWM scoring in 66% of LV segments (varying from 72% at the apex to 56% in the distal diaphragmatic segment). The present work shows exact agreement in RWM scoring in 64% of LV segments (varying from 86% at the proximal antero-lateral segment to 48% at the proximal diaphragmatic segment).

Previous authors (Brady et al, 1979; Harris et al, 1981) correctly draw attention to the problems of using the RAO view caused by right-ventricular (RV) overlap. This makes identification of RWM along the diaphragmatic surface of the left ventricle less reliable. Our findings confirm that RWM is less reliably assessed in the diaphragmatic segments than in the antero-lateral segments, but clearly show that the level of accuracy is adequate. Comparison of proximal diaphragmatic RWM shows agreement to within one scoring point in 90% of cases.

We have not found the LPO view helpful. It has poor interobserver variability (Fig. 4). Agreement between the two observers occurs in about 86% of cases, but this is particularly poor at the proximal segments where agreement between the observers falls to 71% and 81%. The average interobserver difference per segment of 0.67 is the worst of any of the techniques used. The agreement with X-ray contrast ventriculography is also poor, with agreement of RWM scores in about 82% of cases (varying from 90% in the distal diaphragmatic segment down to 76% in the antero-lateral segments). The mean difference per segment for the RWM scores from the two techniques is 0.72. This level of disagreement for the RWM scores between the two techniques is significantly worse than the RAO 30° method (0.56) but better than the first-pass method (0.82).

It is important to recognise that the inaccuracies of the different nuclear techniques compared with X-ray ventriculography arise from different sources.

In the 30° RAO equilibrium gated technique the problem is one of right-ventricular overlap, so that the recognition of LV abnormalities is modified by overlying RV RWM. This can be seen to some extent from the data given in Table I. Six out of 42 diaphragmatic segments show a difference between X-ray ventriculography and radionuclide investigation of greater than one scoring point. In all six, X-ray ventriculography shows a more severe RWM abnormality.

In the LPO equilibrium gated view the problem is still one of RV overlap (though now the right ventricle lies distal to the left), compounded by a greater distance between the camera and the heart.

In the RAO 30° first-pass technique, the inaccuracies between X-ray ventriculography and radionuclide ventriculography arise for different reasons. These would include lack of counts, incomplete mixing, poor bolus quality and so on. As shown in Table I, two studies out of 21 yielded unsatisfactory data and were rejected. The poorest agreement between radionuclide and X-ray ventriculography is at the apex of the left ventricle. This would support the findings of Walton et al (1983), that the left ventricle is a poor mixing chamber and pools of relative stasis exist at the apex of both normal and abnormal ventricles.

First-pass and equilibrium radionuclide ventriculography have different sources of error. The findings presented in this paper serve only to show how each method compares with the accepted gold standard, X-ray ventriculography.

We believe that the best view to complement the accepted LAO 45° view is the RAO 30° view. Furthermore, we believe that equilibrium techniques are satisfactory and that first-pass studies do not add significantly to the results obtained. The use of more esoteric views, such as the LPO view, in equilibrium gated studies should be discouraged.

REFERENCES

BRADY, T. J., THRALL, J. H., LO, K., WALTON, J. A., BRYMER, J. F. & PITT, B., 1979. Excercise ventriculography; comparison of right anterior oblique wall motion analysis between radionuclide and contrast ventriculography (abstract). *Journal of Nuclear Medicine, 20*, 640–641.

DYMOND, D. S., JARRITT, P. H., BRITTON, K. E. & SPURRELL, R. A. J., 1979. Detection of postinfarction left ventricular aneurysms by first pass radionuclide ventriculography using a multicrystal gamma camera. *British Heart Journal, 41*, 68–78.

FOLLAND, E. D., HAMILTON, G. W., LARSON, S. M., KENNEDY, J. W., WILLIAMS, D. L. & RITCHIE, J. L., 1977. The radionuclide ejection fraction: a comparison of three radionuclide techniques with contrast angiography. *Journal of Nuclear Medicine, 18*, 1159–1166.

HARRIS, D. N. F., TAYLOR, D. N., OGILVIE, B. C., GARVIE, N. W., WATKINS, J., ACKERY, D. M. & CONWAY, N., 1981. Left ventricular segmental wall motion—a comparison between equilibrium radionuclide angiography and contrast angiography. *British Journal of Radiology, 54*, 296–301.

KELLY, M. J., GILES, R. W., SIMON, T. R., BERGER, H. J., LANGOU, R. A., ZARET, B. L. & WACKERS, F. J. T., 1981. Multigated equilibrium radionuclide angiocardiography: improved detection of left ventricular wall motion abnormalities and aneurysms by the addition of the left lateral view. *Radiology, 139*, 167–173.

LANE, S. D., PATTON, D. D., STAAB, E. V. & BAGLAN, R. J., 1971. Simple technique for rapid bolus injection. *Journal of Nuclear Medicine, 13*, 118–119.

PACHINGER, O., OGRIS, E., PROBST, P., JOSKOWICS, G., SOCHOR, H., KAINDL, F., 1979. Assessment of left ventricular performance and myocardial viability using quantitative radioisotope techniques. *British Heart Journal, 42*, 205–213.

PICHLER, M., 1978. Noninvasive assessment of segmental left ventricular wall motion: its clinical relevance in detection of ischaemia. *Clinical Cardiology, 1*, 173–191.

TAYLOR, D. N., 1981. Ph.D. Thesis, University of Southampton.

WINZELBERG, G. G., 1980. Scintigraphic evaluation of left ventricular aneurysm. *American Journal of Cardiology, 46*, 1138–1143.

WALTON, S., BROWN, N. J. G., JARRITT, P. H., ELL, P. J. & EMANUEL, R. W., 1983. Regional variation of left ventricular transit times in normal ventricles and those with abnormalities of contraction. *British Heart Journal, 49*, 388–392.

Book reviews

Oncologic Imaging. Ed. by D. G. Bragg, P. Rubin and J. E. Youker, pp. vi+644+index, 1985 (Pergamon Press, New York), $125 (approx. £90).
ISBN 0–08–033653–1

This large and impressive book with its 27 authors (in addition to the three editors) is held together by a rigid aherence to a set format in which each of the anatomically divided chapters making up the body of the book is laid out in a set pattern: an introduction, a section on tumour behaviour and pathology, the local pattern of spread, classification and staging, imaging procedures and assessment (complete with flow charts and a table of staging capability and cost-benefit ratio), imaging strategies and decisions, treatment decisions, the impact of new technology, and references. The book also has initial chapters on the staging and classification of cancer and imaging strategies and four chapters at the end on paediatric oncology, computed tomography and treatment planning, interventional radiology in the diagnosis and management of cancer patients, and the impact of future technology.

Webster's dictionary defines oncology as "the study of tumors", but this book confines itself very largely to malignant tumours. In the head and neck, for instance, there is no mention of angiofibromas nor of inverting papillomas of the nose, both oncologic entities of interest in the region. The rigid format imposes a pattern of repetition which becomes tedious since each author has to ponder on the possible impact of magnetic resonance and digital vascular imaging, while few talk about the effects of clinical signs and biochemical tests on patterns of investigation, and radiological signs are at a premium, presumably because they do not fit into the framework. In a book so fearful of being behind the times the absence of mention of ultrasound in prostatic and rectal carcinomas or of Doppler in the breast strikes an interesting note.

The quality of production is superb and few errors appear. Figures A and B on page 168 are reversed, and "complement" is wrongly spelt several times. The book is an enormous compendium of knowledge which will find its place on the shelves of diagnostic X-ray departments in oncological and radiotherapy centres as a reference source, but does not lend itself to easy or casual reading.

W. D. JEANS

Progress in Clinical and Biological Research Vol. 24. Human Markers and Their Significance. Ed. by T. Dao, A. Brodie and C. Ip, pp. xii+140+index, 1986 (Alan R. Liss, New York), £28.00.
ISBN 0–8451–5054–5

This slim volume consists of the proceedings of a workshop held in Spring 1985. There is no doubt that there are many possible tumour markers for clinical use in breast cancer. The problem for the jobbing oncologist is to sort out which, if any, he should be routinely using in his practice. We are now in the monoclonal age and this is reflected clearly in the proceedings of the workshop.

The excellent introductory chapter by Ceriani discusses the role of circulating mammary epithelial antigens as markers in this disease. The concept that antibodies raised against normal milk-fat globule membranes can be of any use in detecting and measuring tumour load in a patient is, at first sight, surprising. However, there is no doubt that these epithelial antigens are elevated in the serum of patients and can prove helpful under certain circumstances. Several longitudinal studies clearly show a good relationship with disease progress with these markers. Glycosyl transferases are shed by many tumours and cause considerable changes in serum proteins. These are considered in several further chapters, although the true clinical role of their measurement is as yet not clear. There are several accounts of biochemical epidemiology of steroid metabolites. The concept that a biochemical pattern of metabolites could be used to identify those patients at risk from developing breast cancer has been extensively studied, although so far no clinical benefit is apparent.

Unfortunately, the standard of the chapters varies considerably. Some contain new information while others are rehashes of previously published data. Furthermore, camera-ready manuscripts are irritating to the reader; in a world of computerisation, it should not take much effort at least to coordinate the use of a single typeface. The book provides a reasonable summary of the current status of this specialised area and should find a niche in the oncology department's library.

KAROL SIKORA

1986, *The British Journal of Radiology*, *59*, 907–910 SEPTEMBER 1986

The importance of radiolabelling human granulocytes with ^{111}In-tropolonate or ^{111}In-2-mercaptopyridine-N-oxide in plasma containing acid-citrate-dextrose

By Heather J. Danpure, Ph.D. and Safiye Osman, M.Sc.

MRC Cyclotron Unit, Hammersmith Hospital, London W12 0HS

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ABSTRACT

When blood cells are radiolabelled in plasma, for example with ^{111}In-tropolonate, the plasma always contains an anticoagulant, usually acid-citrate-dextrose (ACD) or heparin. The effect of ACD and heparin on the labelling efficiency (LE) and optimum concentration of ligand required to radiolabel human granulocytes in plasma with ^{111}In-tropolonate or ^{111}In-2-mercaptopyridine-N-oxide (^{111}In-merc) has been measured. The concentrations of ligand (tropolone or merc) required for maximum cell labelling in plasma containing ACD were 4×10^{-4} M tropolone and 1×10^{-4} M merc, whereas using plasma containing heparin, the optimum concentrations were 10-fold higher, at 4×10^{-3} M and 1×10^{-3} M respectively. At the optimum ligand concentrations, the LE for 1×10^{8} granulocytes labelled in plasma containing ACD was 90% using ^{111}In-tropolonate and 82% using ^{111}In-merc, whereas using plasma containing heparin they were 68% and only 20%, respectively. Addition of ACD to heparinised plasma abolished the necessity for more ligand and increased the LE to the same values as those for plasma containing ACD alone. These results clearly demonstrate that to obtain a high LE using the lowest possible concentrations of tropolone or merc, the granulocytes must be labelled in plasma containg ACD.

Many hospitals in the UK now radiolabel human leucocytes with ^{111}In-tropolonate in plasma rather than with ^{111}In-oxinate or ^{111}In-acetylacetonate (^{111}In-acac) in saline or buffer because clinical studies have shown that labelling leucocytes in plasma is preferable to labelling them in saline (Peters et al, 1983; Saverymuttu et al, 1983; McAfee et al, 1984). The procedure that was developed for radiolabelling human leucocytes in plasma with ^{111}In-tropolonate (Danpure et al, 1982) used acid-citrate-dextrose (ACD) to anticoagulate the blood, and plasma containing ACD as the labelling medium. But heparin is also widely used to anticoagulate blood, in which case plasma plus heparin would be used as the labelling medium. This paper reports the effect of labelling human granulocytes with ^{111}In-tropolonate and ^{111}In-2-mercaptopyridine-N-oxide (^{111}In-merc) in plasma containing heparin and compares the results with those using plasma containing ACD. The optimum concentrations of ligand (tropolone or merc) required for cell labelling, the labelling efficiency (LE) and the stability of the ^{111}In in the labelled granulocytes were measured.

MATERIALS AND METHODS

Cell separation

Fresh human venous blood from healthy volunteers was anticoagulated with either heparin sodium (mucous) at 15 IU/ml or ACD NIH Formula A (1.5 volumes of ACD to 8.5 volumes of blood). Cell-free plasma for labelling the cells was obtained by centrifuging a portion of the blood at 2000*g* for 10–15 min. "Crude" leucocytes were isolated from blood anticoagulated with ACD as previously described (Danpure et al, 1982) except that hydroxyethyl starch (Plasmasteril) was used instead of dextran. Granulocytes were isolated from "crude" leucocytes using a modification of the two-step discontinuous Percoll-saline density gradients previously reported (Saverymuttu et al, 1983). The gradients contained 2 ml aliquots of 80% and 65% v/v isotonic Percoll in saline and were centrifuged at 400*g* for 5 min.

Cell labelling

Determination of optimum ligand concentrations. 1×10^{7} granulocytes in 0.9 ml aliquots of plasma containing ACD or heparin were labelled for 15 min at 37°C with 0.1 ml ^{111}In-tropolonate containing 18.5 kBq (0.5 μCi) ^{111}In and 10^{-1} to 4×10^{-4} M tropolone (Fluka) or 10^{-1} to 10^{-4} M 2-mercaptopyridine-N-oxide (sodium salt, Fluka) in Hepes-saline buffer, pH 7.6. 1×10^{7} granulocytes were also labelled in 0.9 ml plasma containing both ACD and heparin at the same concentrations as those used to anticoagulate the blood. After labelling, the granulocytes were washed twice with 9 ml isotonic saline by centrifugation at 100*g* for 5 min. The activity in the cells and supernatants was measured and the LE calculated.

Labelling efficiencies. To determine the effect that the anticoagulant would have on the LE in a clinical situation, 1×10^{8} granulocytes were labelled as described above in 1 ml plasma containing ACD or heparin with ^{111}In complexed to the appropriate optimum concentration of tropolone or merc.

Stability of the ^{111}In on the labelled cells. Granulocytes that were labelled with the optimum concentrations of tropolone or merc were washed free of unbound ^{111}In and resuspended in 1 ml cell-free plasma containing ACD or heparin and incubated for 1 h at 37°C to measure the amount of ^{111}In eluted from the labelled cells.

RESULTS

Figure 1 shows that the optimum concentration of tropolone for labelling granulocytes with ^{111}In-tropolonate in plasma plus heparin was 4×10^{-3} M, 10 times greater than the 4×10^{-4} M required for optimal labelling of granulocytes in plasma containing ACD. There was a similar 10-fold difference in optimum ligand concentration using ^{111}In-merc. The optimum concentration of merc using plasma plus heparin was 1×10^{-3} M compared with 1×10^{-4} M using plasma plus ACD. However, when granulocytes were labelled in plasma containing both heparin and ACD, the optimum concentrations of tropolone and merc were the same as those for plasma plus ACD, namely 4×10^{-4} M tropolone and 1×10^{-4} M merc.

Besides the difference in the optimum ligand concentrations in the two labelling media, there was also a difference in the amount of ^{111}In incorporated by the cells. With each of the two ^{111}In-complexes, the LE in plasma plus heparin was much lower than that in plasma plus ACD. In a given medium ^{111}In-tropolonate always gave a higher LE than ^{111}In-merc.

TABLE I

EFFECT OF ANTICOAGULANT ON THE OPTIMUM LIGAND CONCENTRATION AND LE FOR 1×10^8 GRANULOCYTES LABELLED IN 1 ML PLASMA WITH ^{111}IN-TROPOLONATE OR ^{111}IN-MERC

Ligand	Labelling medium			
	Plasma + ACD		Plasma + heparin	
	Optimum ligand concentration (M)	LE	Optimum ligand concentration (M)	LE
Tropolone	4×10^{-4}	90%	4×10^{-3}	68%
Merc	1×10^{-4}	82%	1×10^{-3}	20%

The effect that ACD and heparin would have on LE in a clinical situation is shown in Table I. With both ^{111}In complexes there was a much higher LE when 1×10^8 granulocytes were labelled in 1 ml plasma containing ACD than in 1 ml plasma containing heparin.

Despite the differences in optimum ligand concentration and LE between plasma containing ACD and

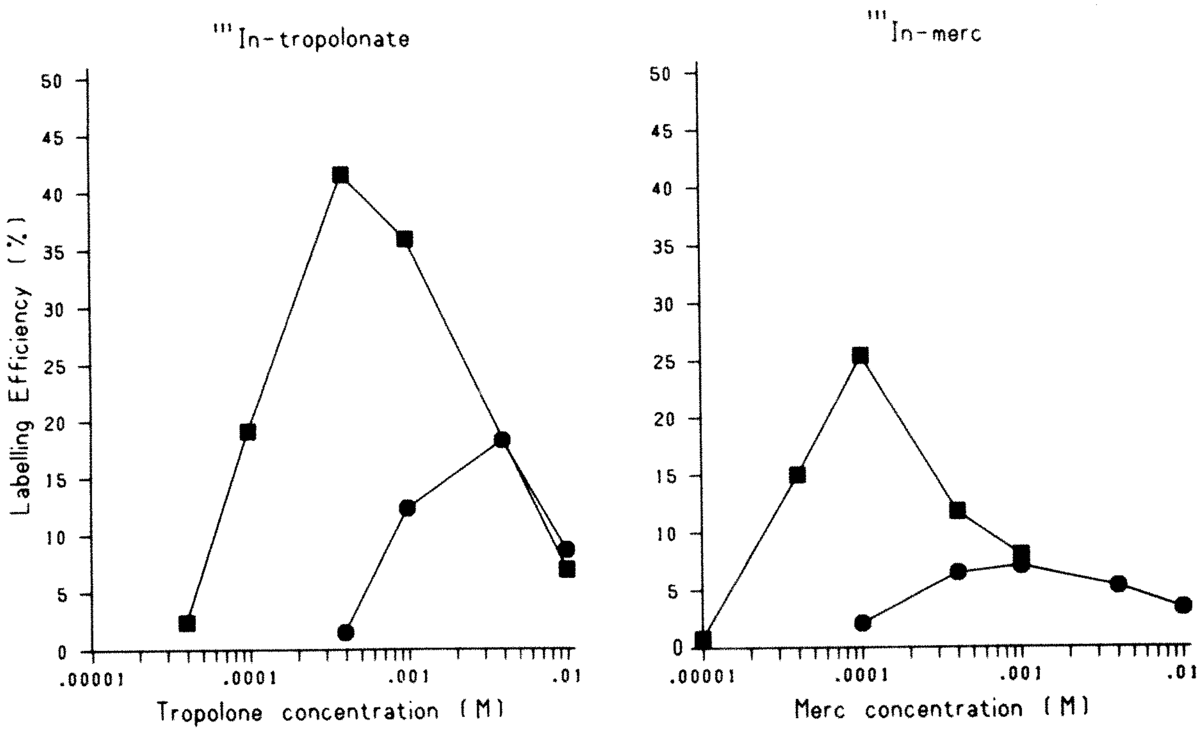

FIG. 1.

The effect of ACD and heparin on the concentration of tropolone and merc required to label 1×10^7 granulocytes with ^{111}In-tropolonate and ^{111}In-merc in plasma plus ACD (■) and plasma plus heparin (●).

plasma containing heparin, the stability of the ^{111}In in the granulocytes was the same in the two labelling media, provided that the cells were labelled with the appropriate optimum concentrations of tropolone or merc. In all cases, less than 3% of the ^{111}In was released during 1 h of incubation in cell-free plasma. The amount of ^{111}In released was unaffected by whether the labelled cells were incubated in plasma plus ACD or plasma plus heparin.

DISCUSSION

This paper shows the importance of radiolabelling human granulocytes with ^{111}In-tropolonate or ^{111}In-merc in plasma that contains the anticoagulant ACD. Plasma containing ACD was preferable to plasma containing heparin as the cell-labelling medium because a 10-fold lower concentration of ligand (tropolone or merc) was required for maximum uptake of ^{111}In when the plasma contained ACD than when it contained heparin. The optimum concentrations were 4×10^{-4} M tropolone and 1×10^{-4} M merc when the plasma contained ACD, but 4×10^{-3} M tropolone and 1×10^{-3} M merc when it contained heparin. Also the LE was much higher when the plasma contained ACD than when it contained heparin. For example, 1×10^{8} granulocytes labelled in 1 ml plasma with ^{111}In-tropolonate gave an LE of 90% when the plasma contained ACD, but only 68% when it contained heparin. The differences were even greater using ^{111}In-merc, where an LE of 82% was obtained using ACD but only 20% using heparin.

Besides the beneficial effect of ACD on cell labelling, Peters et al (1986) also found that ACD prevented the aggregation of human leucocytes when they were isolated from whole blood, whereas heparin did not. They therefore recommend that ACD be used to anticoagulate blood, irrespective of whether the leucocytes are subsequently labelled in plasma or in a plasma-free medium. Others (Coleman et al, 1980; Goodwin et al, 1980) have, however, reported no difficulties in labelling leucocytes in saline or buffer from blood anticoagulated with heparin.

Of the three initial studies which reported the use of ^{111}In-tropolonate as a cell-labelling agent, only two (Dewanjee et al, 1981; Danpure et al, 1982) reported that it would label blood cells in plasma. In both of these studies the cells were labelled in plasma containing ACD. In the third study, Burke et al (1982) failed to label leucocytes with ^{111}In-tropolonate in plasma containing heparin. This was probably because the optimum concentration of tropolone for labelling cells in plasma containing heparin is 100-fold greater than that required to label cells in buffer (Dewanjee et al, 1981; Burke et al, 1982; Danpure & Osman, 1984). Even when the optimum concentration of tropolone is used, the LE in plasma containing heparin is much lower than it is in plasma containing ACD, as shown in this paper.

The mode of action of ACD and heparin on the uptake of ^{111}In-complexes into leucocytes incubated in plasma is not known. Thakur et al (1985) found that 10 times more merc was required to label leucocytes in plasma containing heparin, and thought that the merc and heparin had reacted to form a disulphide which could not bind metal ions. Although this may explain our results with merc, it does not explain those with tropolone, because tropolone does not contain any sulphur atoms. It does not, however, rule out a different interaction between heparin and tropolone. But heparin could equally well exert its effect by reacting with ^{111}In, the ^{111}In-complex, the plasma constituents or directly with the cells. Whatever the mechanism, the effect of heparin on cell labelling was inhibited by ACD because the same results were obtained when leucocytes were labelled in plasma containing both ACD and heparin as those in plasma containing ACD alone.

From a clinical point of view, where the aim is to achieve a viable population of cells which have been labelled with a high LE using the lowest possible concentration of ligand, this paper clearly demonstrates that human leucocytes should be labelled with ^{111}In-tropolonate or ^{111}In-merc in plasma containing ACD, not in plasma containing heparin.

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REFERENCES

BURKE, E. T., ROATH, S., ACKERY, D. & WYETH, P., 1982. The comparison of 8-hydroxyquinoline, tropolone and acetylacetone as mediators in the labelling of polymorphonuclear leucocytes with In-111: a functional study. *European Journal of Nuclear Medicine, 7*, 73–76.

COLEMAN, R. E., WELCH, D. M., BAKER, W. J. & BEIGHTOL, R. W., 1980. Clinical experience using ^{111}In-labelled leucocytes. In *^{111}In-labelled Neutrophils, Platelets and Lymphocytes*. Ed. by M. L. Thakur & A. Gottschalk (Trivirum, New York), pp. 103–118.

DANPURE, H. J. & OSMAN, S., 1984. Labelling blood cells with ^{111}In-tropolonate. In *Blood Cells in Nuclear Medicine, Part II. Migratory Blood Cells*. Ed. by G. F. Fueger (Nijhoff, Boston), pp. 161–179.

DANPURE, H. J., OSMAN, S. & BRADY, F., 1982. The labelling of blood cells in plasma with ^{111}In-tropolonate. *British Journal of Radiology, 55*, 247–249.

DEWANJEE, M. K., RAO, S. A. & DIDISHEIM, P., 1981. ^{111}In-tropolone, a new high-affinity platelet label: preparation and evaluation of labelling parameters. *Journal of Nuclear Medicine, 22*, 981–987.

GOODWIN, D. A., DOHERTY, P. W. & MCDOUGALL, I. R., 1980. Clinical use of ^{111}In-labelled white cells: an analysis of 312 cases. In *^{111}In-labelled Neutrophils, Platelets and Lymphocytes*. Ed. by M. L. Thakur & A. Gottschalk (Trivirum, New York), pp. 131–150.

MCAFFEE, J. G., SUBRAMANIAN, G. & GAGNE, G., 1984. Techniques of leucocytes harvesting and labelling: problems and perspectives. *Seminars in Nuclear Medicine, 14*, 83–106.

PETERS, A. M., SAVERYMUTTU, S. H., DANPURE, H. J. & OSMAN, S., 1986. Cell labelling. In *Methods in Haematology, 12 Radionuclides in Haematology*. Ed. by S. M. Lewis & R. J. Bayly (Churchill Livingstone, Edinburgh), pp. 79–109.

PETERS, A. M., SAVERYMUTTU, S. H., REAVY, H. J., OSMAN, S. & LAVENDER, J. P., 1983. Imaging of inflammation with ^{111}In-tropolonate labelled leucocytes. *Journal of Nuclear Medicine*, *24*, 39–44.

SAVERYMUTTU, S. H., PETERS, A. M., DANPURE, H. J., REAVY, H. J., OSMAN, S. & LAVENDER, J. P., 1983. Lung transit of ^{111}In-labelled granulocytes. *Scandinavian Journal of Haematology*, *30*, 151–160.

THAKUR, M. L., MCKENNY, S. L. & PARK, C. H., 1985. Evaluation of ^{111}In-2-mercaptopyridine-N-oxide for labelling leucocytes in plasma: A kit preparation. *Journal of Nuclear Medicine*, *26*, 518–523.

Book review

Positron Emission Tomography and Autoradiography: Principles and Applications for the Brain and Heart. Ed. by M. E. Phelps, J. C. Mazziotta and H. R. Schelbert, pp. xii+690, 1986 (Raven Press, New York), $98.50 (approx. £66.00).

ISBN 0-88167-118-5

The major characteristic of this book which differentiates it from previous texts on positron emission tomography (PET) is the standard of technical information given in each section over and above the normal descriptive methods relating to the use of PET in medicine. The book covers in great detail the basic physiology of the brain and the heart and describes both autoradiographic and PET applications in the study of these organs.

Two chapters on cerebral circulation, metabolism and protein synthesis and coronary circulation describe in detail the biochemical functions of the brain and heart. There is much technical information, but these sections make very good reading for anyone wishing to study cerebral or cardiac diseases. The chapters on receptors in the brain and myocardial metabolism are highly technical for the non-specialist, but give much of the basic background needed to understand how pharmaceuticals localise in the brain and myocardium. There is an interesting chapter on single and multiple radionuclide autoradiography which gives a clear and comprehensible description of the techniques and some descriptive information relating to the scanning systems and the accuracy obtainable.

The section on PET principles and quantification is again an excellent, clear, and simple description of the physical technique of PET, sufficiently detailed for the physicist and probably comprehensible to others working in the field. The discussion of tracer kinetic modelling used to determine the parameters obtained in PET studies related to brain and myocardial metabolism contains examples to show how the relevant parameters are arrived at and a subsequent section relates to the accuracy with which these parameters can be estimated. This part contains a simple exposition of statistics, a topic usually omitted from these texts.

There are sections on positron-emitter labelled compounds and biochemical principles in radiopharmaceuticals which tie in well with the earlier chapters on receptors and metabolism. They provide an extensive reference for cyclotron-related pharmaceuticals and a good review of clinical strategies. The final two chapters in the book are more conventional to this kind of text, covering PET studies of the brain and the myocardium. However, the excellent quality and detail of the information highlights perfectly the value of PET and the images have survived the photographic process unusually well.

The message of this book appears to be that physicians will understand more about brain and myocardial function from PET and autoradiography than from any other single technique presently available, including magnetic resonance imaging. It is hard to see, with the sensitivity that the latter possesses, the quantitative accuracy of PET being challenged in the near future and the spatial resolution now available is competitive with that obtained with current anatomical techniques.

We highly recommend not only those working in the field, but those who would understand more of the function of the brain and the heart, to read this book.

R. J. OTT
J. BABICH

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A comparison of the tumour concentrations obtainable with misonidazole and Ro 03-8799

By S. Dische, M.D., F.R.C.R., M. I. Saunders, M.D., F.R.C.R., *M. H. Bennett, M.A., M.B., B.Chir., F.R.C. Path., E. P. Dunphy, M.B.B.S., F.R.C.R., C. Des Rochers, B.Sc., S.R.N., †M. R. L. Stratford, Ph.D., †A. I. Minchinton, B.Sc. and †P. Wardman, Ph.D.

Marie Curie Research Wing, Regional Radiotherapy and Oncology Centre, *Pathology Department and †Gray Laboratory, Cancer Research Campaign, Mount Vernon Hospital, Northwood, Middlesex HA6 2RN

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ABSTRACT

Both Ro 03-8799 and misonidazole were administered to six patients before tumour sampling. Using similar doses, tumour concentrations of Ro 03-8799 were approximately double those of misonidazole. Examination of the data with regard to the relative sensitising efficiencies of these two compounds gives us, as a conservative estimate, a factor of 1.6 in favour of Ro 03-8799. From these observations it is predicted that, when given with radiotherapy in a 25-fraction course Ro 03-8799, is likely to be at least five times more effective as a hypoxic cell sensitiser than misonidazole.

In a programme of research directed to the introduction of an hypoxic cell radiosensitiser which could be given in a more effective dose than misonidazole, the Roche experimental drug, Ro 03-8799, was given to normal volunteers and then to patients in 1981 (Saunders et al, 1982). The expectation of a more rapid urinary excretion and a shorter half-life of 5–6 h was attained. Evidence in six patients where tumour biopsies were performed confirmed the prediction that this basic compound would concentrate in tumour.

Phase I studies of Ro 03-8799, performed at Mount Vernon and at Cambridge, showed that the dose-limiting toxicity was an immediate effect upon the central nervous system which gave rise to feelings of heat and malaise and which was associated with sweating. These effects, however, always completely subsided, leaving no persistent problem. An incidence of hypersensitivity skin reactions of approximately 12% has led to the drug being discontinued in these cases, but apart from this and occasional nausea, no other toxic effect has been observed (Roberts et al, 1984; Saunders et al, 1984). The peripheral neuropathy observed in patients given other nitroimidazoles such as misonidazole, desmethylmisonidazole, metronidazole and SR-2508, has not been detected in patients given Ro 03-8799. A dose limit of 1 g/m^2 of surface area has been set for dose administrations, which should be no more frequent than three times weekly, and 0.75 g/m^2 of surface area for daily administration five times weekly. Extensive sampling of tumour and normal tissues at 10–25 min after administration has shown that tumour concentrations are, on the average, 3.4 times greater than those in the plasma at the time of biopsy. Normal tissues show lower concentrations with a mean of 1.9 times greater than those in the plasma, with the exception of the brain where the uptake is similar to that found in tumour (Roberts et al, 1984).

The tumour concentrations achieved vary from case to case and from sample to sample. These variations can be related to the structure of the tumour sample being examined (Dische et al, 1977; Rich et al, 1981). Necrotic areas must be expected to show low concentration of drug; in addition, tumour samples contain, besides tumour cells, supporting connective tissue and adjacent tissues such as skin, mucosa and subcutaneous fat. These normal tissues have been shown to contain a lower concentration of Ro 03-8799 (Saunders et al, 1984). The exact make-up of the sample sent for analysis is, therefore, important in the interpretation of the result obtained and our established practice with the sensitising drugs is to separate a portion of every specimen for histological study.

It follows that only a limited credence can be given to an historic comparison of tumour concentrations achieved in patients given a new sensitiser with those obtained previously when misonidazole was given. For this reason when we investigated Ro 05-9963 as a radiosensitiser we gave it together with misonidazole before tumour sampling (Dische et al, 1981). We have now administered both misonidazole and Ro 03-8799 to patients arranging the timing of the administration so that at the moment of biopsy the optimum intervals between administration and time for radiotherapy had elapsed for both drugs.

METHOD AND MATERIALS

Samples were obtained from six patients with advanced, recurrent or metastatic tumours. In two of three patients with carcinoma of cervix the primary tumour was biopsied while in the third a metastatic subcutaneous nodule was removed. A patient with carcinoma of the vulva underwent drill biopsy of an inguinal node. In one patient with malignant melanoma a subcutaneous metastasis was removed while in another an axillary node was sampled by drill biopsy.

A capsule of misonidazole containing 500 mg was administered orally 3.5–4 h before time of biopsy and Ro 03-8799 in a similar dose of 500 mg was given intravenously over a period of 5 min, starting between 12 min and 24 min prior to biopsy. All the patients included gave their informed consent and, with these doses, no side-effects were observed. At the time of biopsy a blood sample was taken for plasma concentration and in most cases blood samples were taken subsequently to determine half-lives. The pharmacokinetics were comparable with the previous findings of a half-life of approximately 11 h for misonidazole and 5.5 h for Ro 03-8799.

Techniques used for measurement of sensitiser concentration

Samples were prepared for analysis in a manner similar to that described by Saunders et al (1982). Drug concentrations were determined by high-performance liquid chromatography (HPLC) using a method which can simultaneously determine both sensitisers and their metabolites, which will be described in detail elsewhere. In the earlier work of Saunders et al (1982), concentrations were expressed in the form of the free base, but subsequently we have given values in terms of the hydrochloride as this is the form in which the drug is administered and it is on this basis that all comparisons of relative efficacy have been made.

A major metabolite of misonidazole is Ro 05-9963 (desmethylmisonidazole). As it is a radiosensitiser, the concentration has been added to that of misonidazole. Ro 31-0313, the *N*-oxide metabolite of Ro 03-8799, is inactive as a radiosensitiser and levels are not reported here.

The histological quantification of the proportion of the different tissues present was made by a simple visual impression gained from an examination under the microscope of a section stained with haematoxylin and eosin.

CASE REPORTS

Case 1

This was a female aged 38 years with a surface area of 1.43 m^2 and Stage III anaplastic squamous carcinoma of the cervix. Biopsies of the cervix were performed. Misonidazole 500 mg was given orally 3 h 56 min before tumour sampling. Ro 03-8799 500 mg was given intravenously over 5 min, commencing 24 min before tumour sampling. Plasma concentrations at time of tumour sampling were:

$$\left.\begin{array}{ll}\text{Misonidazole} & 13.3\\ \text{Ro 05-9963} & 1.7\end{array}\right\}\ 15.0\ \mu\text{g/ml}$$

Ro 03-8799 5.9 μg/ml

Tumour concentrations are given in Table I.

TABLE I

CASE 1. TUMOUR CONCENTRATIONS

Sample	Histological assessment			Miso + Ro 05-9963 (μg/g)	Tissue/ plasma ratio	Ro 03-8799 (μg/g)	Tissue/ plasma ratio
	Tumour (%)	Stroma (%)	Necrosis (%)				
1	75	20	5	9.9	0.66	17.8	3.02
2	60	40	0	12.2	0.81	16.8	2.85
3	60	10	30	18.4	1.23	25.3	4.29
4	20	20	60	6.25	0.42	7.5	1.27
5	10	30	60	2.87	0.19	2.8	0.47
6	30	40	30	1.64	0.11	1.5	0.25
7	0	0	100	0.2	—	—	—

Miso = misonidazole.

Seven "tumour" samples were analysed. One contained only necrotic debris and no appreciable concentration of either sensitiser. The first three samples contained a majority of tumour and showed the expected concentrations of misonidazole and Ro 03-8799. Samples 4, 5 and 6 contained considerable necrotic debris and concentrations of both drugs were lower, particularly with Sample 6. It seemed quite possible that in these specimens the small portion sent for histological study may not have been representative of the whole and that much of the material may have been totally necrotic.

Case 2

This was a female aged 63 years with a surface area of 1.64 m^2 and a poorly differentiated squamous-cell carcinoma of the cervix. Biopsies of cervix were performed. Misonidazole 500 mg was given orally 3 h 38 min before tumour sampling and Ro 03-8799 500 mg was given intravenously over 5 min, commencing 15 min before tumour sampling. Plasma concentrations at time of tumour sampling were:

$$\left.\begin{array}{ll}\text{Misonidazole} & 12.7\\ \text{Ro 05-9963} & 1.3\end{array}\right\}\ 14.0\ \mu\text{g/ml}$$

Ro 03-8799 6.1 μg/ml

Tumour concentrations are given in Table II.

Both samples of tumour appeared to contain a high density of tumour cells and the concentration of Ro 03-8799 was three times greater than that of misonidazole. A third specimen showed histologically only vaginal mucosa with *in situ* carcinoma and, although the concentration of misonidazole was similar to that in the other two samples, that of Ro 03-8799 was considerably lower.

Case 3

This was a female aged 74 years with a surface area of 1.46 m^2 and a poorly differentiated squamous carcinoma of the vulva. Drill biopsy of a node in the groin was carried out. Misonidazole 500 mg was given orally 3 h 55 min before tumour sampling and Ro 03-8799 500 mg was given intravenously over 5 min commencing 20 min before tumour sampling. Plasma concentrations at time of tumour sampling were.

$$\left.\begin{array}{ll}\text{Misonidazole} & 15.1\\ \text{Ro 05-9963} & 1.7\end{array}\right\}\ 16.8\ \mu\text{g/ml}$$

Ro 03-8799 6.1 μg/ml

Tumour concentrations are given in Table III.

TABLE II

CASE 2: TUMOUR CONCENTRATIONS

Sample	Histological assessment			Miso + Ro 05-9963 (μg/g)	Tissue/ plasma ratio	Ro 03-8799 (μg/g)	Tissue/ plasma ratio
	Tumour (%)	Stroma (%)	Necrosis (%)				
1	90		10	12.2	0.87	39.2	6.4
2				13.5	0.96	40.4	6.6
3	*			13.5	0.96	25.1	4.1

Miso = misonidazole

*Vaginal mucosa with *in situ* carcinoma.

TABLE III

CASE 3: TUMOUR CONCENTRATIONS

Sample	Histological assessment Tumour (%)	Stroma (%)	Necrosis (%)	Miso + Ro 05-9963 (μg/g)	Tissue/plasma ratio	Ro 03-8799 (μg/g)	Tissue/plasma ratio
1	25		75	22.0	1.31	25.2	4.1
2	2		98	7.3	0.43	1.8	0.30

Miso = misonidazole.

The material removed by drill biopsy showed much necrosis; one sample did contain about 25% tumour, but the other contained a few scattered tumour cells in otherwise necrotic material. In this latter specimen a very low concentration of both sensitisers was obtained.

Case 4

This was a female aged 54 years with a surface area of 1.66 m^2 and a poorly differentiated squamous-cell carcinoma of the cervix. Biopsies of cervix were performed. Misonidazole 500 mg was given orally 3 h 43 min and 3 h 50 min before tumour sampling. Ro 03-8799 500 mg was given intravenously over 5 min commencing 12 min and 19 min before tumour sampling. Plasma concentrations at time of tumour sampling were:

$$\left.\begin{array}{ll}\text{Misonidazole} & 13.4\\ \text{Ro 05-9963} & 1.2\end{array}\right\} 14.6\ \mu\text{g/ml and } \left.\begin{array}{l}13.4\\ 1.2\end{array}\right\} 14.6\ \mu\text{g/ml}$$

Ro 03-8799 14.0 μg/ml 9.8 μg/ml

Tumour concentrations are given in Table IV.

Stroma dominated in the histological sections of all four samples and tumour was not observed in two. Concentrations of Ro 03-8799 and "tissue"/plasma ratios resembled those seen in normal tissues.

Case 5

This was a female aged 80 years, surface area 1.65 m^2, with malignant melanoma. A subcutaneous metastasis was surgically removed. Misonidazole 500 mg was given orally 3 h 13 min before tumour sampling and Ro 03-8799 500 mg was given intravenously over 5 min commencing 15 min before tumour sampling. Plasma concentrations at time of tumour sampling were:

$$\left.\begin{array}{ll}\text{Misonidazole} & 15.0\\ \text{Ro 05-9963} & 1.1\end{array}\right\} 16.1\ \mu\text{g/ml}$$

Ro 03-8799 6.8 μg/ml

Tumour concentrations are given in Table V.

TABLE IV

CASE 4: TUMOUR CONCENTRATIONS

Sample	Histological assessment Tumour (%)	Stroma (%)	Necrosis (%)	Miso + Ro 05-9963 (μg/g)	Tissue/plasma ratio	Ro 03-8799 (μg/g)	Tissue/plasma ratio
1*	10	90		13.6	0.93	26.2	1.87
2†		100		13.8	0.95	18.1	1.85
3†	10	90		12.3	0.84	22.3	2.28
4†		100		13.3	0.91	21.3	2.17

Miso = misonidazole.

*Taken 12 min after Ro 03-8799 administration commenced.

†Taken 19 min after Ro 03-8799 administration commenced.

TABLE V

CASE 5: TUMOUR CONCENTRATIONS

Sample	Histological assessment Tumour (%)	Stroma (%)	Necrosis (%)	Miso + Ro 05-9963 (μg/g)	Tissue/plasma ratio	Ro 03-8799 (μg/g)	Tissue/plasma ratio
1		100*		5.6	0.35	6.1	0.90
2		100*		5.5	0.34	3.9	0.57
3	85	15		11.0	0.68	19.4	2.85
4				11.4	0.71	28.3	4.16
5		100*		4.6	0.29	4.4	0.65

Miso = misonidazole.

*Adipose tissue.

The excised subcutaneous metastasis of malignant melanoma showed a high concentration in a specimen which comprised 85% tumour cells. Three samples of subcutaneous fat contained only half the concentration of misonidazole and approximately a quarter of the concentration of Ro 03-8799 when compared with the tumour samples.

Case 6

This was a male aged 67 years, surface area 1.75 m^2, with malignant melanoma. A drill biopsy of the axillary node was performed. Misonidazole 500 mg was given orally 3 h 30 min before tumour sampling. Ro 03-8799 500 mg was given intravenously over 5 min commencing 15 min before tumour sampling. Plasma concentrations at time of tumour sampling were:

$$\left.\begin{array}{ll}\text{Misonidazole} & 10.7\\ \text{Ro 05-9963} & 0.9\end{array}\right\} 11.6\ \mu\text{g/ml}$$

Ro 03-8799 5.9 μg/ml

Tumour concentrations are shown in Table VI.

Only a small sample was obtained by drill biopsy of an axillary node in this second case of malignant melanoma. Tiny fragments sent for histological study showed fat only, but the main sample appeared, by naked eye examination, to be of tumour and the relatively high concentrations of Ro 03-8799 would be compatible with this.

The mean concentrations seen in the six cases where tumour was either confirmed histologically or, as in one case, considered clinically certain, are shown in Table VII. The mean of 0.9 seen with misonidazole is in the range of previous observations, though near its upper end when allowance is made for the inclusion of Ro 05-9963 levels (Dische et al, 1981). The tumour/plasma ratio of 3.8 for Ro 03-8799 is similar to that reported previously (Saunders et al, 1984).

TABLE VI

CASE 6: TUMOUR CONCENTRATIONS

Sample	Histological assessment Tumour (%)	Stroma (%)	Necrosis (%)	Miso + Ro 05-9963 (μg/g)	Tissue/plasma ratio	Ro 03-8799 (μg/g)	Tissue/plasma ratio
1		100		11.5	0.99	26.8	4.54

Miso = misonidazole.

TABLE VII

MEAN CONCENTRATIONS AND TUMOUR/PLASMA RATIOS IN SAMPLES CONTAINING TUMOUR

Case	No of samples	Misonidazole		Ro 03-8799		Ratio: Ro 03-8799/ misonidazole in tumour (ratio c : a)
		In tumour (µg/g) (a)	Tumour/ plasma ratio (b)	In tumour (µg/g) (c)	Tumour/ plasma ratio (d)	
1	6	8.5	0.57	12.0	2.0	1.41
2	2	12.9	0.92	39.8	6.5	3.10
3	1	22.0	1.31	25.2	4.1	1.15
4	2	13.0	0.91	24.3	2.4	1.87
5	2	11.2	0.70	23.9	3.5	2.12
6	1	11.5	0.99	26.8	4.5	2.33
Mean		13.2	0.90	25.3	3.8	2.00

DISCUSSION

In this series of six patients with malignant tumours, four squamous-cell carcinomas and two malignant melanomas, the predicted pattern of tumour uptake for the two sensitisers has been demonstrated. Approximately twice the concentration has been attained with Ro 03-8799 as with misonidazole in these patients who were given 500 mg of both drugs.

We do not know whether the concentrations of sensitiser obtained in tumour reflect those in the hypoxic cells, but there is evidence that the critical population of the hypoxic, though potentially viable, tumour cells are sited in the histologically intact portion of the tumour, well clear of any area showing necrosis (Chapman et al, 1983). The drugs under study are freely diffusible and are likely to penetrate to such areas. Furthermore, it seems unlikely that there are differences related to the different sensitisers which could influence the comparative observations made.

Previous discussions concerning the improvement in therapeutic ratio likely with Ro 03-8799 compared with misonidazole have considered tumour/plasma ratios and absolute tumour concentrations (Saunders et al, 1984, Roberts et al, 1986). We now have measurements of tumour concentrations of both radiosensitisers in the same tumour sample, greatly enhancing the validity of the comparison.

Three factors need to be considered when comparing two sensitisers, in this case Ro 03-8799 and misonidazole (Table VIII).

1. The tolerated doses for the radiotherapy regime which is to be employed.
2. The tumour concentrations achieved when the two drugs are given in equal doses.
3. The sensitising efficiencies.

For misonidazole, the tolerable dose of 12 g/m^2 of surface area is determined by the cumulative toxicity,

TABLE VIII

A COMPARISON OF THE RELATIVE THERAPEUTIC RATIOS OF MISONIDAZOLE AND RO 03-8799 TO BE EXPECTED WHEN GIVEN AS HYPOXIC CELL RADIOSENSITISERS IN FRACTIONATED RADIOTHERAPY

	10 treatments Miso	Ro 03-8799	25 treatments Miso	Ro 03-8799
1) Route	oral	i.v	oral	i.v
2) Total permitted dose (g/m^2)	12.0	10.0	12.0	18.75
3) Dose per treatment (g/m^2)	1.2	1.0	0.48	0.75
4) Relative dose per treatment	1.0	0.83	1.0	1.56
5) Relative concentrations achieved with equal doses (Table VII)	1.0	2.0	1.0	2.0
6) Relative tumour concentrations which can be expected (row 4 × row 5)	1.0	1.66	1.0	3.12
7) Relative concentrations for equal efficacy*	1.0	1.6	1.0	1.6
8) Relative therapeutic ratio (row 6 × row 7)	1.0	2.7	1.0	5.0

Miso = misonidazole.

*Factor 1.6 appropriate when doses and tumour concentrations are expressed as weights (corresponds to 2.3 in molar terms, see Appendix).

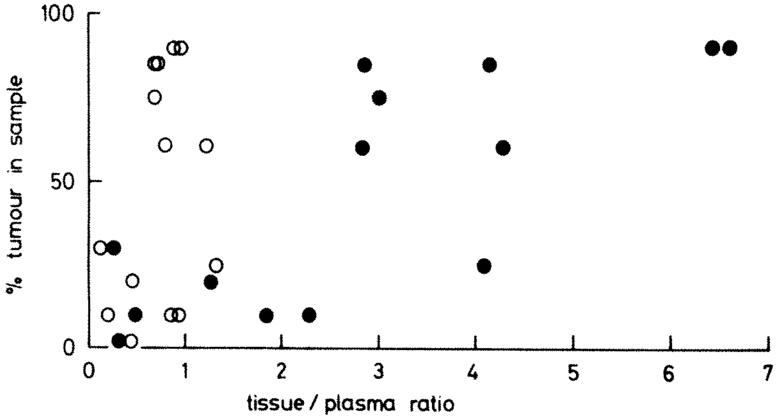

FIG. 1.

The tissue/plasma ratios for Ro 03-8799 (●) and for misonidazole (○) have been plotted against the percentage of the sample occupied by tumour cells as observed histologically. We have excluded Sample 3, Case 2, which showed *in situ* carcinoma in vaginal mucosa.

but for Ro 03-8799, because the toxicity is acute and not cumulative, total dose is limited by the fractionation employed, either 1 g/m^2 of surface area when the drug is given on alternate days or 0.75 g/m^2 when given more frequently in a daily regime. Thus, the relative benefit of Ro 03-8799 over misonidazole will be increased with the number of fractions (Row 4, Table VIII).

Relative tumour concentrations (Row 6) are calculated as the product of the relative tolerable dose (Row 4) and the ratio in tumour of Ro 03-8799 to misonidazole after administration of equal doses (Row 5).

We must recognise that in human tumours a relationship exists between the tissue/plasma ratio of Ro 03-8799 and the proportion of the sample occupied by tumour cells: this is not seen with misonidazole (Fig. 1). In samples containing only a small percentage of tumour cells, tissue/plasma ratios similar to those obtained in normal tissues were found. It is probable that the concentration actually in the tumour cells in those samples is higher and similar to those in samples where tumour cells dominate. Our figure of 2.00 for the relative concentrations in tumour for the two drugs is, therefore, likely to be an underestimate.

In previous discussions concerning the relative sensitising efficiencies of the two drugs at the concentrations likely to be achieved in hypoxic tumour cells in man, factors ranging from 1.0 to 2.5 have been considered (Saunders et al, 1984; Roberts et al, 1986). In the Appendix we have considered the evidence and have concluded that the ratio could be 1.6. This, a conservative estimate, is used in Row 7 of Table VIII. The product of this and the tumour concentrations gives us a predictor of the relative therapeutic ratio (Row 8).

The prediction of an improvement over misonidazole by a factor of 5 in a 25-fraction regime is likely to be an underestimate for the reasons given above and gives much encouragement to further clinical work with Ro 03-8799 and the initiation of randomised controlled trials in selected tumour types and stages.

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REFERENCES

ADAMS, G. E., FLOCKHART, I. R., SMITHEN, C. E., STRATFORD, I. J., WARDMAN, P. & WATTS, M. E., 1976. Electron affinic sensitization. A correlation between structures, one-electron reduction potentials and efficiencies of nitroimidazoles as hypoxic cell radiosensitizers. *Radiation Research*, *67*, 9–20.

ADAMS, G. E., CLARKE, E. D., FLOCKHART, I. R., JACOBS, R. S., SEHMI, D., STRATFORD, I. J., WARDMAN, P., WATTS, M. E., PARRICK, J., WALLACE, R. G. & SMITHEN, C. E., 1979. Structure activity relationships in the development of hypoxic cell radiosensitizers. I. Sensitization efficiency. *International Journal of Radiation Biology*, *35*, 133–150.

ADAMS, G. E., AHMED, I., FIELDEN, E. M., O'NEILL, P. & STRATFORD, I. J., 1980. The development of some nitroimidazoles as hypoxic cell sensitizers. In *Radiation Sensitizers: Their Use in the Clinical Management of Cancer*. Ed. by L. W. Brady (Masson, New York), pp. 33–38.

CHAPMAN, J. D., FRANKO, A. J. & KOCH, C. J., 1983. The fraction of hypoxic clonogenic cells in tumor population. In *Biological Bases and Clinical Implications of Tumor Radioresistance*. Ed. by G. Fletcher, C. Nervi & R. Withers (Masson, New York), pp. 61–73.

DENNIS, M. F., STRATFORD, M. R. L., WARDMAN, P. & WATTS, M. E., 1985. Cellular uptake of misonidazole and analogues with acidic or basic functions. *International Journal of Radiation Biology*, *47*, 629–643.

DISCHE, S., SAUNDERS, M. I., LEE, M. E., ADAMS, G. E. & FLOCKHART, I. R., 1977. Clinical testing of the radiosensitizer Ro 07-0582: experience with multiple doses. *British Journal of Cancer*, *35*, 567–579.

DISCHE, S., SAUNDERS, M. I., RILEY, P. J., HAUCK, J., BENNETT, M. H., STRATFORD, M. R. L. & MINCHINTON, A. I., 1981. The concentration of desmethylmisonidazole in human tumours and in cerebro-spinal fluid. *British Journal of Cancer*, *43*, 344–349.

RICH, T. A., DISCHE, S., SAUNDERS, M. I., STRATFORD, M. & MINCHINTON, A., 1981. A serial study of the concentration of misonidazole in human tumours correlated with histologic structure. *International Journal of Radiation Oncology, Biology, Physics, 7*, 197–203.

ROBERTS, J. T., BLEEHEN, N. M., WORKMAN, P. & WALTON, M. I., 1984. A phase I study of the hypoxic cell radiosensitizer Ro 03-8799. *International Journal of Radiation Oncology, Biology, Physics, 10*, 1755–1758.

ROBERTS, J. T., BLEEHEN, N. M., WALTON, M. I. & WORKMAN, P., 1986. A clinical phase I toxicity study of Ro 03-8799: plasma, urine, tumour and normal brain pharmacokinetics. *British Journal of Radiology, 59*, 107–116.

ROSS, W. J. C., 1961. Increased sensitivity of the Walker tumour towards aromatic nitrogen mustards carrying basic side chains following glucose pretreatment. *Biochemical Pharmacology, 8*, 235–240.

SAUNDERS, M. I., DISCHE, S., FERMONT, D., BISHOP, A., LENOX-SMITH, I., ALLEN, J. G. & MALCOLM, S. L., 1982. The radiosensitizer Ro 03-8799 and the concentration which may be achieved in human tumours—a preliminary study. *British Journal of Cancer, 46*, 706–719.

SAUNDERS, M. I., DISCHE, S., ANDERSON, P. J., TOTHILL, M., STRATFORD, M. R. L. & MINCHINTON, A. I., 1984. The clinical testing of Ro 03-8799—pharmacokinetics, toxicology, tissue and tumour concentrations. *International Journal of Radiation Oncology, Biology, Physics, 10*, 1759–1763.

SMITHEN, C. E., CLARKE, E. D., DALE, J. A., JACOBS, R. S., WARDMAN, P., WATTS, M. E. & WOODCOCK, M., 1980. Novel (nitro-1-imidazolyl) alkanolamines as potential radiosensitizers with improved therapeutics properties. In *Radiation Sensitizers: Their Use in the Clinical Management of Cancer*. Ed. by L. W. Brady (Masson, New York), pp. 22–32.

WARDMAN, P., 1975. Protonation of the radical-anions of nitro-imidazole radiosensitizers and the formation of radical adducts. *International Journal of Radiation Biology, 28*, 585–588.

——1982. Molecular structure and biological activity of hypoxic cell radiosensitizers and hypoxic specific cytotoxins. In *Advanced Topics on Radiosensitizers of Hypoxic Cells*. Ed. by A. Breccia, C. Rimondi & G. E. Adams. NATO Advanced Study Institute Series A: Life Sciences, Vol. 43 (Plenum Press, New York), pp. 49–75.

WATTS, M. E., ANDERSON, R. F., JACOBS, R. S., PATEL, K. B., WARDMAN, P., WOODCOCK, M., MOAZZAM, M., PARRICK, J. & WALLACE, R. G., 1980. Evaluation of novel hypoxic cell radiosensitizers *in vitro*. In *Radiation Sensitizers: Their Use in the Clinical Management of Cancer*. Ed. by L. W. Brady (Masson, New York), pp. 175–185.

WILLIAMS, M. V., DENEKAMP, J. D., MINCHINTON, A. I. & STRATFORD, M. R. L., 1982. *In vivo* assessment of basic 2-nitroimidazole radiosensitizers. *British Journal of Cancer, 46*, 127–137.

APPENDIX: ESTIMATION OF THE LIKELY RELATIVE EFFICACY OF MISONIDAZOLE AND RO 03-8799 AS RADIOSENSITISERS

We can estimate relative equieffective concentrations via three *independent* routes (a) predictions based upon measured chemical properties and previously established relationships between these properties and efficacy, (b) predictions from *in-vitro* measurements, taking into account measured extracellular/intracellular concentration gradients, and (c) predictions from mouse tumour models.

(a) *Prediction based upon chemical properties*

Adams et al (1976, 1979) quantified the "electron-affinity relationship" between radiosensitisation efficiency (*e.g.* the extracellular concentration, C required to obtain a defined enhancement ratio with mammalian cells *in vitro*) and electron affinity (*e.g.* the reduction potential E vs NHE for the sensitiser/radical-anion couple at pH 7). The relationship between C and E is of the form:

$$-\log C = b_0 + b_1 E \qquad (1)$$

and, if C is in mol/kg and E is in V, then the slope b_1 of the redox relationship (Equation (1)) was found to be *c.* 7.0–8.2 V^{-1} for enhancement ratios (SER) of 1.4–1.6. Values of E for misonidazole and Ro 03-8799 of −0.389 and −0.346 V, respectively, at pH 7 have been reported (Adams et al, 1976; Smithen et al, 1980). The pH-dependence of E is well understood, for misonidazole, E is invariant within 0.005 V for all pH > 6.3 (Wardman, 1975) and measurements with Ro 03-8799 (Clarke & Wardman, unpublished) show that E does not vary by more than ±0.005 V between pH 6.3 and 8.3, cf RGW-603 (Wardman, 1982).

Hence, Ro 03-8799 is more electron-affinic than misonidazole by 0.043 V in the physiological pH range. Using $b_1 = 7.6\ V^{-1}$ we calculate an expected ratio of concentrations required to achieve the same effect for misonidazole relative to Ro 03-8799 of 2.1 ($= 10^{0.043 \times 7.6}$), at an SER of 1.5.

(b) *Prediction based on* in-vitro *measurements*

Smithen et al (1980) and Watts et al (1980) measured the radiosensitisation efficiencies of Ro 03-8799 and misonidazole, respectively, using V79-379A Chinese hamster fibroblasts *in vitro* under similar conditions, and found that Ro 03-8799 was *c.* 10 times more efficient a radiosensitiser than misonidazole in terms of the extracellular concentrations required to achieve similar responses.

These comparisons have been repeated in numerous experiments by Watts et al (unpublished) since 1977–78. The relationship between SER and extracellular concentration is a smooth curve when the concentration is plotted on a logarithmic scale and, indeed, for SER ⩽ 1.6, SER increases practically linearly with log C with many compounds. Hence, it is appropriate to average and discuss sensitiser efficacy in terms of log C. Twelve separate sets of experiments by Watts et al since 1978, using misonidazole and V79-379A cells, yield log $C = -3.422 \pm 0.031$ and -3.048 ± 0.026 for an SER of 1.4 and 1.6, respectively, where C is in mol/dm^3 = mol/kg and all uncertainties are standard errors (SE). Corresponding values from eight sets of experiments for Ro 03-8799 between 1977 and 1981 give log $C = -4.47 \pm 0.11$ and -4.067 ± 0.089 for an SER = 1.4 and 1.6, respectively.

These data from numerous experiments yield estimates of the difference in efficacy of misonidazole and Ro 03-8799 (in terms of extracellular concentrations) of $\Delta\log C = 1.05 \pm 0.11$ and 1.02 ± 0.09 at the SER level of 1.4 and 1.6, respectively. Thus, the initial report of an order-of-magnitude higher efficiency of Ro 03-8799 compared to misonidazole (*extracellular* concentrations) has been confirmed on numerous occasions, the pooled data at the SER level of 1.4 corresponding to a factor of 11.1 and ±1 SE representing the range 8.6–14.5 (10.4, 8.4–13.0 at an SER of 1.6).

For better comparison with tissue measurements, these factors need to be corrected for extracellular intracellular concentration gradients, long anticipated (*e.g.* Ross, 1961) and measured with the compounds of interest here using mammalian cells *in vitro* (Dennis et al, 1985). Using the same conditions and cells as the radiosensitiser measurements, Dennis et al measured extracellular : average intracellular concentration ratios for misonidazole and Ro 03-8799 of

0.68 ± 0.03 and 3.28 ± 0.09, respectively; Ro 03-8799 concentrates within the cells by a factor of 4.80 ± 0.23 compared with misonidazole. Using this latter factor, the relative efficacy of Ro 03-8799 compared with misonidazole, when expressed in terms of *average intracellular* concentrations, becomes 2.3 (±1 SE, range 1.8–3.0) at the SER level of 1.4 (2.2, 1.8–2.7 at an SER of 1.6).

The corrected relative efficacy factor of 2.2–2.3 is similar to the factor of 2.1 predicted from the difference in electron affinity (see above). It is likely that the uncertainty limits quoted overestimate the degree of uncertainty. Radiosensitisation efficiency is remarkably insensitive to variation in molecular properties other than reduction potential and factors which control intracellular uptake (Wardman, 1982). Of the many (> 60) analogues of Ro 03-8799 examined in the *in-vitro* assay by Watts et al (Adams et al, 1980; Smithen et al, 1980; Watts et al, unpublished), the majority are close analogues with $pK_a > 8$ and of moderate lipophilicity. All such analogues were closely similar to Ro 03-8799 in their radiosensitising properties *in vitro*; numerous neutral analogues of misonidazole are indistinguishable from the prototype. These observations lend further support to the observations already made with Ro 03-8799 and misonidazole *in vitro*.

(c) Prediction based on in-vivo *measurements*

A comparison of Ro 03-8799 and misonidazole in radiosensitising a mouse fibrosarcoma (SA Fab) was made by Williams et al (1982), using tumour growth delay as end-point. With both compounds, three sets of measurements were made with average tumour concentrations in the range of most clinical relevance: *c.* 0.05–3.00 mmol/kg misonidazole and 0.05–0.2 mmol/kg Ro 03-8799, with the SER in the range *c.* 1.2–1.5. (With both compounds, one measurement was made at the lower end of the range and two grouped at the higher end.) Interpolating from the plot of SER vs log C gives estimated tumour concentrations required to achieve an SER of 1.5 of *c.* 0.41 and 0.21 mmol/kg for misonidazole and Ro 03-8799, respectively, *i.e.* Ro 03-8799 appears to be *c.* 1.9 times as efficient as misonidazole at the SER level of 1.5.

While a twofold higher efficiency of Ro 03-8799 compared with misonidazole would be consistent with either of the two independent predictions above, it is easy to overinterpret data of this type. The estimates of Williams et al (1982) typically had uncertainties (SE) of ±0.15 in the associated SER. The implications of such uncertainties have been noted by Wardman (1982). An increase of about 2.6 times in sensitiser concentration is needed to increase SER from 1.4 to 1.6 with compounds of $E \simeq -0.37$ V *in vitro* (Adams et al, 1979); the increase in SER with increasing concentration derived from the data of Williams et al (1982), d(SER)/d(log C) is about 0.3–0.4 over the range noted above. These values imply that an uncertainty in the measurement of the SER of ±0.15 corresponds to an uncertainty in estimating the concentration required to achieve a defined response which is well in excess of the factor of ~2, the difference predicted for Ro 03-8799 and misonidazole. Much more data need to be obtained before reasonably precise estimates of the relative efficacy of the two compounds at clinically relevant concentrations can be derived from these experiments.

Conclusions

The best estimate of the relative efficacy of Ro 03-8799 and misonidazole, at enhancement ratios/concentrations within the clinically realistic range, is that derived from *in-vitro* measurements, after correcting for relative, average intracellular concentrations. Ro 03-8799 is probably a factor ~2.3 more efficient than misonidazole when expressed in molar concentrations required to achieve the same response. The relative molar mass of Ro 03-8799 is 1.445 or 1.264 times higher than that of misonidazole when the former is expressed as the hydrochloride salt or free base, respectively, so that the factor is reduced to ~1.6 or 1.8 if concentrations are expressed as weight of the hydrochloride or free base, respectively, rather than moles. Predictions based upon chemical properties and on *in-vivo* measurements are quite consistent with the above estimate.

It should be stressed that both *in-vitro* and *in-vivo* data suggest the relative efficacy of Ro 03-8799 to misonidazole *increases* if comparison is made at concentration/responses higher than those used in this analysis. Thus, interpolation of the data of Williams et al (1982) yields a factor of *c.* 3.2 in molar terms for the relative efficacy of Ro 03-8799 compared with misonidazole at the SER level of 1.8. A response of SER = 1.5 requires average intracellular concentrations of 0.11 mmol/kg Ro 03-8799 in V79-379A cells *in vitro* or *c.* 0.22 mmol/kg in the mouse fibrosarcoma. Tumour levels of 0.2 mmol/kg (58 μg/g Ro 03-8799 as hydrochloride or 51 μg/g as free base) are expected to be *frequently* exceeded at individual administered dose levels of 750–1000 mg/m^2 tolerated in multifraction regimes. (The six cases described in the present study gave a mean tumour concentration of 25 μg/g after a dose of 500 mg; at a dose of 0.75 g/m^2 and surface area of 1.7 m^2, a tumour concentration of 65 μg/g Ro 03-8799 hydrochloride would be expected.) The above estimate of relative efficacy is, therefore, conservative.

Book reviews

Advances in the Biosciences Vol. 55. Germ Cell Tumour II. Ed. by W. G. Jones, A. Milford Ward and C. K. Anderson, pp. xv + 496 + index, 1985 (Pergamon Press Ltd, Oxford), £57.00.
ISBN 0-08-031997-1

This publication is of the proceedings of the second Germ Cell Tumour Conference held at the University of Leeds in April 1985, and, like the previous account of the first Conference held in 1981, the editors are to be congratulated on producing their book so rapidly.

The individual contributors to the Conference came from all over Europe as well as North America, and thus one receives an excellent international review of current thought on germ cell tumours. Some aspects of the histopathology of both the primary and metastatic tumours are well discussed, although the illustrations are not clearly displayed. Some interesting ideas on flow cytometry are described, and, rightly, there is a great emphasis placed on the role of tumour markers in early management, their response to chemotherapy and, in particular, on their importance when a surveillance policy is being followed. The latter subject is well covered and particular emphasis is given to the dangers of pursuing such policies without a meticulously high standard of follow-up being available. There is even a fascinating chapter on the financial implications of such a policy, although it is a pity that the author did not appear to get his facts right—a computed tomographic scan costs at least £200, not £75 as stated, and a course of radiotherapy if properly costed should be nearer £400 than £100. Chemotherapy is covered in great detail, but the figures and tables are really quite difficult to follow. Although radiotherapy is not now such an important part of treatment, some more detailed discussion of techniques and management would have been welcome. The surgical management and the extragonadal tumours are well covered, as are the problems of infertility. It is a pity that the chapters (which are not numbered) and the one-page discussions are somewhat mixed up in content, but presumably this is how the Conference was presented chronologically.

It is difficult to know for whom the book is intended; certainly not for the radiotherapist in training, as the factual matter is probably far too detailed for easy digestion and the very small print does not make for easy reading. As a textbook, however, consultant radiotherapists and medical oncologists will find it an excellent reference book, and it could have a place in most departmental libraries.

H. F. HOPE-STONE

The Fundamentals of X-Ray and Radium Physics, 7th edit. By Joseph Selman, xxxiii + 592 + index, 1985 (Charles C. Thomas, Springfield, Illinois), $29.75.
ISBN 0-398-05065-1

This book has found a place on many a library shelf since it was first published over 30 years ago. The seventh edition shows a small increase in overall length, while a glance through the contents section suggests the changes are very superficial. The author has contented himself with the title and kept to the fundamentals of his subject, starting the book with simplified mathematics at a junior-school level and progressing slowly through basic physics, electricity and magnetism. The second quarter, dealing with X rays and their production, is very adequate, biased heavily to diagnostic equipment, the only references to radiotherapy being developed out of a discussion on absorbed dose and a later section on radiation protection. One sentence acknowledges the use of the gray as the new unit of absorbed dose while the rest of the text adheres rigidly to the use of roentgens and rads.

The production of the X-ray image is covered in the third quarter. Starting with the composition of the film and the design of a (wet) darkroom, the author elaborates on the chemistry of both manual and automated processing, the definition of radiographic quality and techniques for improving that quality. Computed tomography has been added to the chapter on special equipment, while the use of 350 kV equipment for chest radiography has been deleted.

The text concludes with a section on radium and radionuclides and a section on radiation protection. Here the revision concentrates more on the Federal regulations than on the ICRP recommendations with which many readers have become more familiar over the last decade.

As a basic text, this book has much to recommend it, but, unfortunately, this latest update has not been as complete as one might have wished and students will need to read more widely before they try to satisfy their examiners. They will undoubtedly benefit both from attempting the questions and problems at the end of each chapter and from the comprehensive index.

C. K. BOMFORD

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The application of the linear-quadratic model to fractionated radiotherapy when there is incomplete normal tissue recovery between fractions, and possible implications for treatments involving multiple fractions per day

By R. G. Dale, Ph.D., C.Phys., F.Inst.P.

Department of Medical Physics, Charing Cross Hospital, Fulham Palace Road, London W6 8RF

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ABSTRACT

By extending a previously developed mathematical model based on the linear-quadratic dose–effect relationship, it is possible to examine the consequences of performing fractionated treatments for which there is insufficient time between fractions to allow complete damage repair. Equations are derived which give the relative effectiveness of such treatments in terms of tissue-repair constants (μ values) and α/β ratios, and these are then applied to some examples of treatments involving multiple fractions per day. The interplay of the various mechanisms involved (including repopulation effects) and their possible influence on treatments involving closely spaced fractions are examined. If current indications of the differences in recovery rates between early- and late-reacting normal tissues are representative, then it is shown that such differences may limit the clinical potential of accelerated fractionation regimes, where several fractions per day are given in a relatively short overall time.

In assessing the doses required to produce tolerable normal-tissue reactions in clinical radiotherapy, the well known semi-empirical models (*e.g.* the Ellis formula, cumulative radiation effect (CRE) and time, dose and fractionation factor (TDF) models) have played an important role. However, such models are only capable of giving reliable results if they are applied within the limits set by the particular clinical data on which they are based (*e.g.* Liversage, 1971). It is now clear that the more recent linear-quadratic (LQ) formulation may be applied to a wider variety of clinical circumstances simply by the careful selection of parameters which are characteristic of particular tissue responses.

The LQ model is so-called on account of the assumed mathematical form of the underlying dose–response equation. The potential usefulness of the model has been discussed by a number of authors (*e.g.* Fowler, 1984a,b), who have demonstrated how the method predicts the improvements in therapeutic ratio which may be obtained by appropriate adjustment of dose per fraction in fractionated radiotherapy. Indeed, the identification of the crucial significance of dose per fraction, as opposed to total dose, has been one of the major achievements of the LQ model.

The implications of the theory to other aspects of modern radiotherapy practice (*e.g.* treatments with permanent or temporary implants, total body irradiations (TBIs), etc.) have been considered in some detail in an earlier paper (Dale, 1985), where equations incorporating the effects of intracellular repair during prolonged irradiation were derived. The purpose of this paper is to extend further the method and apply it to some examples of treatments involving closely spaced fractions. Thames (1984) has suggested that repair rates may differ between normal tissues, and the implications of this also are examined.

BASIC CONSIDERATION OF THE LQ MODEL

The model postulates that gross radiation effects (E) may be related to fractional radiation dose (D_N) given in N fractions by:

$$E = N(\alpha D_N + \beta D_N^2) \qquad (1)$$

A number of articles have dealt with the steps leading to the derivation of Equation (1) (*e.g.* Barendsen, 1982). The mode of cellular death which is responsible for the observed effect is inherently assumed to be of the two-hit type, and in applying Equation (1) we further assume that biological effect is correlated with the surviving fraction of target cells (Thames et al, 1982), although it is acknowledged that the equivalence is not exact (Michalowski, 1984).

Dale (1985) has shown that it is convenient to think in terms of there being two distinct components which lead to cell death, one being due to simultaneous damaging of two adjacent targets (the α component), the other due to the union of independently damaged targets (the β component). Whether or not the targets themselves are the individual strands of the DNA helix (as suggested by Chadwick and Leenhouts (1973)) is not relevant to the mathematical analysis.

Hendry and Moore (1985) show how absolute values of α and β may be derived from dose–incidence data, but the particular usefulness of all LQ equations relies on the fact that particular radiation effects may be characterised by specific α/β ratios (Fowler, 1984b). An individual knowledge of both α and β is not required in the application of the equations to calculating changes in treatment schedules.

There are now emerging some general indications of the α/β values which can be used in clinical problem solving:

(a) Acute epithelial tissue reactions in radiotherapy tend to be characterised by relatively high α/β ratios, typically in the range 8–13 Gy and with an average of about 10 Gy (Fowler, 1984b).

(b) Late-tissue reactions tend to be characterised by relatively low α/β ratios, typically in the range 2–6 Gy, but the spread of values may extend outside this range (Fowler, 1984b).

(c) Tumour responses tend to be characterised by high α/β ratios, typically 10–25 Gy (Fowler, 1984b; Williams et al, 1985).

Barendsen (1982) introduced two very useful concepts which ease the manipulation of LQ equations. He defined the extrapolated response dose (ERD) to be the hypothetical dose which is required for a given radiation effect when an infinite number of infinitely small fractions is given. A quantity called relative effectiveness per unit dose (RE), which is dependent on the α/β ratio characteristic of the effect under consideration, may also be defined for any particular regime. For fractionated radiotherapy, RE is related to dose/fraction (D_N) by the relationship:

$$\mathrm{RE} = 1 + D_N(\beta/\alpha) \qquad (2)$$

The ERD and RE are related to total dose (TD) by:

$$\mathrm{ERD} = \mathrm{TD} \times \mathrm{RE} \qquad (3)$$

In general, regimes are iso-effective on a specific tissue if they produce the same ERD, therefore two regimes A and B are considered iso-effective if:

$$(\mathrm{TD})_A \times (\mathrm{RE})_A = (\mathrm{TD})_B \times (\mathrm{RE})_B \qquad (4)$$

Dale (1985) has shown how the ERD and RE concepts may be developed and applied to any type of treatment, not only fractionated radiotherapy. By repeated use of Equation (4) it is possible to find a range of regimes which are iso-effective to a particular reference regime, *i.e.* the equation is very useful in the construction of iso-effect curves (Dale, 1986; O'Donoghue, 1986). Although the mathematical relationships which define RE can be quite complex, the basic equations linking RE with ERD and total dose, *i.e.* Equations (3) and (4), make it easy to follow how the LQ model is operating when different regimes are being compared.

In order to deal with those cases where irradiation times are long enough to allow some degree of intracellular recovery during treatment, Dale (1985) considered separately the two modes by which it is assumed that lethal radiation damage may be created. Type A damage is that due to the α component, and Type B damage is that due to the β component. It is important to appreciate that Type A damage is always directly proportional to the dose delivered, irrespective of the rate of delivery. Type B damage, because it is caused by an interaction between the separately damaged components of a target doublet, is dependent on dose-rate. This is the main reason for invoking the concepts of Type A and Type B damage and considering them separately, since RE values for *any* type of radiation regime may be calculated from:

$$\mathrm{RE} = 1 + \frac{\text{Total Type B damage}}{\text{Total Type A damage}} \qquad (5)$$

It is useful to remember Equations (3)–(5).

THE EFFECT OF THE TIME FACTOR IN THE LQ MODEL

The main aim of this paper is to examine applications of the LQ model to treatments involving closely spaced fractions. The necessary mathematics is a development of that used in the analysis of protracted radiotherapy and, since this has already been covered in detail elsewhere (Dale, 1985), these new equations should be seen in conjunction with the earlier work. The analysis parallels an approach originally due to Roesch (1978), which has been utilised in slightly different form by a number of other authors (*e.g.* Douglas, 1982a,b; Thames, 1985).

Of particular interest is the independently developed "incomplete-repair" model of Thames (1985), who used the linear quadratic cell survival curve to give the log surviving fraction of cells after closely spaced fractions. Although presented in a different form, the equations of Thames are fundamentally the same as those to be derived here, and to those already published for fractionated and protracted regimes (Dale, 1985). However, the equations of Thames do not incorporate the effects of exponentially falling dose-rates associated with decaying sources.

In Thames' approach the emphasis is on the derivation of equations giving the log surviving fraction for different regimes. A particular advantage of this approach is that the model can be very elegantly applied to the analysis of tissue repair kinetics as determined by experimental data. By equating surviving fractions (and by assuming that "iso-survival = iso-effect"), the interplay of the LQ parameters may also be investigated.

In Dale's approach, the emphasis is mainly on the derivation of RE values, which can then be used directly (*via* Equations (3) and (4)) in clinical problem solving. The fact that the ERD concept is clearly identified and utilised as a basis for determining equivalence is a further aid, since there are obvious parallels between the use of the ERD in LQ equations and of the nominal standard dose (NSD) in the Ellis equation, with which many clinicians are very familiar. Although ERD and NSD are quite different, they each act as a conceptual fulcrum in their respective models. The use of ERD also allows the establishment of important equivalence relationships which are independent of α/β.

To proceed further with the analysis, consider a fractionated regime consisting of individual irradiations of short duration T, delivered at dose-rate R, and time x

apart. Let p be the (small) probability per unit dose that one target in a doublet is hit. In the first fraction:

$$\text{Probability (sublethal damage per target doublet)} = 2pRT$$

Since p is small, we assume that the amount of Type B damage created in any fraction does not significantly reduce the amount of sublethal damage present (*i.e.* p^2 is negligible). At the second fraction, time x after the first, assuming that this sublethal damage repairs exponentially with time constant μ, then

$$\text{Probability (sublethal damage remaining per doublet)} = 2pRT\exp(-\mu x)$$

Therefore,

$$\text{Probability (creating sublethal damage in time } dt \text{ at time } t \text{ into irradiation)} = \varepsilon[2pRt+2pRT\exp(-\mu x)]pR\,dt$$

where ε is the probability that two damaged target pairs interact to produce lethal damage.

If n is the number of target pairs then, in time T, Type B damage is given by:

$$2n\varepsilon p^2R^2\int_0^T[t+T\exp(-\mu x)]\,dt = \beta R^2T^2[1+2\exp(-\mu x)] \qquad (6)$$

where (following Dale, 1985) $\beta = n\varepsilon p^2$.

Equation (6) gives the amount of Type B damage created in the second fraction. By extending the argument, it may be shown that the total Type B damage produced in the Nth fraction is:

$$\beta R^2T^2[1+2\exp(-\mu x)+2\exp(-2\mu x)+\ldots+2\exp\{-(N-1)\mu x\}]$$

Therefore, since $RT = D_N$, the dose per fraction, the total Type B damage created in N such fractions is:

$$\beta D_N^2(N+2[(N-1)\exp(-\mu x)+(N-2)\exp(-2\mu x)+\ldots+\exp\{-(N-1)\mu x\}]) = \beta D_N^2\left[N+2\sum_{i=1}^{N-1}(N-i)\exp(-i\mu x)\right] \qquad (7)$$

The expression inside the square brackets may be further reduced (see Appendix I), *i.e.* total Type B damage in N fractions

$$= \beta D_N^2\left\{\frac{N(1-K^2)-2K(1-K^N)}{(1-K)^2}\right\} \qquad (8)$$

where $K = \exp(-\mu x)$. Equation (8) above is contained within Equation (7) of Thames, 1985.

For N such fractions total Type A damage is given by $N\alpha D_N$. Therefore, utilising Equation (5) of this paper we have:

$$\text{RE} = 1+\left(\frac{\beta}{\alpha}\right)\left(\frac{D_N}{N}\right)\left\{\frac{N(1-K^2)-2K(1-K^N)}{(1-K^2)}\right\} \qquad (9)$$

As a simple check on Equation (9) it may be noted that if x is large, $K\rightarrow 0$, *i.e.* for conventionally fractionated regimes,

$$\text{RE} = 1+D_N(\beta/\alpha) \qquad (10)$$

This is the standard result for normally fractionated regimes (Dale, 1985).

Application to Treatments Involving Multiple Fractions Per Day

In order to standardise terminology, two main types of treatment involving multiple fractions per day (MFD treatment) may be identified (Thames et al, 1983).

Accelerated fractionation (*AF*) where overall time is shorter than in conventional treatment, achieved by giving two or three daily fractions. Total dose and fraction size are similar to those given in conventional treatments.

Hyperfractionation (*HF*) where fraction doses are smaller than conventional doses, but are given two or three times daily to achieve an increase in the total dose, which is given in a conventional overall time.

These definitions are used because they have been utilised by other authors and are convenient for the analysis. However, it should be remembered that there are other possible types of MFD treatments which may not fall within the above constraints relating to fraction size and overall time, but which nevertheless could have important treatment potential.

The application of the equations derived above will be considered with reference to some practical examples, initially using a value of $\mu = 0.46\ \text{h}^{-1}$, corresponding to a repair half-life of 1.5 h This is the figure adopted by Liversage in his formulations (Liversage, 1969a,b) and which has been shown to be applicable to late-reacting tissues by Thames (1984). For these initial assessments the possible effects of tissue repopulation will be ignored.

Consider first a treatment which delivers 60 Gy in 30 fractions, *i.e.* $D_N = 2$ Gy. If the fractions are well apart then, from Equation (10),

$$\text{RE} = 1+2\ (\beta/\alpha)$$

If the fractions are at intervals of 6 h then, from Equation (9),

$$\text{RE} = 1+2.26\ (\beta/\alpha)$$

Similarly, at intervals of 4 h,

$$\text{RE} = 1+2.73\ (\beta/\alpha)$$

and at intervals of 2.7 h,

$$\text{RE} = 1+3.55\ (\beta/\alpha)$$

Therefore RE increases as the interval between fractions decreases, the numerical value depending on the α/β ratio characteristic of the end-point in question.

In practice, fractions in such a regime could well be given at intervals between around 9 a.m. and 6 p.m. There would thus be a relatively long interval (~15 h) between fractions on successive days. During this period virtually all the accumulated damage would repair, therefore the *effective* RE of such treatments may be more appropriately calculated by applying Equation (9) to each *daily* treatment regime. If this is done, then, for two fractions at intervals of 6 h,

$$\mathrm{RE} = 1+2.13\ (\beta/\alpha)$$

and, for three fractions at intervals of 4 h,

$$\mathrm{RE} = 1+2.46\ (\beta/\alpha)$$

and, for four fractions at intervals of 2.7 h,

$$\mathrm{RE} = 1+3.08\ (\beta/\alpha).$$

Thus, the working RE values in such practical regimes are lower than those in which the fraction intervals are kept constant throughout. Nevertheless, the general trend of increasing RE with reduced fraction spacing is the same as before.

It is one of the fundamental predictions of the LQ model (e.g. Fowler, 1984a) that late-reacting tissue damage in a fractionated regime may be reduced relative to early-reacting tissue damage by reducing the dose per fraction. However, as the above reasoning indicates, the situation will be complicated if the fraction intervals are insufficient to allow full repair of damage between fractions. An additional problem in assessing the magnitude of such effects is the likelihood that the damage repair rates will vary among tissues, as will the extent of repopulation in response to injury. Thames (1984) has reported that the half-life of recovery in early-reacting tissues may be smaller than in late-reacting tissues, with skin as an exception. Assuming values which have been found to be representative ($T_{1/2} = 0.5$ h for early-reacting tissues, 1.5 h for late-reacting tissues), it is possible tentatively to re-assess the potential benefits of AF and HF treatments.

The above sequence of calculations was for doses per fraction of 2 Gy, *i.e.* a conventional level which would be found in AF type treatments. In HF type treatments the doses per fraction would be less than this; a figure of 1 Gy will be a useful value to take for subsequent analyses.

The results are given in Table I. It is assumed in all cases that the ERD required is that for a regime delivering 60 Gy in 30 fractions, *i.e.* 72 Gy and 108 Gy for early- and late-reacting tissues, respectively (calculated via Equations (3) and (10)). The table highlights the necessary calculation steps (using Equation (9)) for different fraction spacings and for the two selected values of dose per fraction.

Considering first the AF treatments (dose/fraction = 2 Gy), it is seen that the total dose required to obtain the same late-reacting damage (*i.e.* with ERD = 108 Gy) decreases markedly with reduced fraction interval, whereas the doses required for similar early-reacting effects (with ERD = 72 Gy) remain virtually constant. Therefore, if tumour α/β values are also high (Fowler, 1984b; Williams et al, 1985), and if

TABLE I

VALUES OF RE AND TOTAL DOSE FOR AF AND HF REGIMES INVOLVING FRACTIONS GIVEN AT SPECIFIED TIME INTERVALS

Regime		Dose/fraction = 2 Gy (accelerated fractionation)		Dose/fraction = 1 Gy (hyperfractionation)	
		Late reactions $\alpha/\beta = 2.5$ Gy $\mu = 0.46\ \mathrm{h}^{-1}$ ERD = 108 Gy	Early reactions $\alpha/\beta = 10$ Gy $\mu = 1.39\ \mathrm{h}^{-1}$ ERD = 72 Gy	Late reactions $\alpha/\beta = 2.5$ Gy $\mu = 0.46\ \mathrm{h}^{-1}$ ERD = 108 Gy	Early reactions $\alpha/\beta = 10$ Gy $\mu = 1.39\ \mathrm{h}^{-1}$ ERD = 72 Gy
Two fractions/day, 6 h intervals	RE (Eq 9)	$1+\frac{2.13}{2.5}=1.85$	$1+\frac{2}{10}=1.20$	$1+\frac{1.07}{2.5}=1.43$	$1+\frac{1}{10}=1.10$
	∴ TD to give (Eq 3)	$\frac{108}{1.85}=58.4$ Gy	$\frac{72}{1.2}=60$ Gy	$\frac{108}{1.43}=75.5$ Gy	$\frac{72}{1.1}=65.4$ Gy
Three fractions/day, 4 h intervals	RE (Eq. 9)	$1+\frac{2.46}{2.5}=1.98$	$1+\frac{2.01}{10}=1.20$	$1+\frac{1.23}{2.5}=1.49$	$1+\frac{1.01}{10}=1.10$
	∴ TD to give (Eq 3)	$\frac{108}{1.98}=54.5$ Gy	$\frac{72}{1.2}=60$ Gy	$\frac{108}{1.49}=72.4$ Gy	$\frac{72}{1.1}=65.4$ Gy
Four fractions/day, 2.7 h intervals	RE (Eq. 9)	$1+\frac{3.08}{2.5}=2.23$	$1+\frac{2.07}{10}=1.21$	$1+\frac{1.54}{2.5}=1.62$	$1+\frac{1.04}{10}=1.10$
	∴ TD to give (Eq. 3)	$\frac{108}{2.23}=48.4$ Gy	$\frac{72}{1.21}=59.5$ Gy	$\frac{108}{1.62}=66.7$ Gy	$\frac{72}{1.1}=65.4$ Gy

the degree of tumour proliferation is unaffected by the reduction in treatment time, equivalent tumour kill effects will only be produced in AF treatments at the expense of extra late-tissue damage, because of the slower repair rate in these latter tissues.

For HF treatments (dose/fraction = 1 Gy) it will be noted from Table I that the expected advantages of smaller doses per fraction continue to outweigh the effects of reduced damage repair between fractions and, provided the number of daily fractions is three or less, sparing of late-tissue damage is likely.

Although the effects of tissue repopulation are outside the scope of the basic LQ model, some account needs to be taken of the phenomenon in deciding between the relative efficacy of HF and AF regimes. Tumour repopulation during treatment will be considered in more detail later since it is obviously of special relevance.

The degree of repopulation occurring in late-responding tissues (with the possible exception of kidney and lung) will be small over the time scale of the treatments under consideration, and can be reasonably discounted.

Modern megavoltage beams allow considerable sparing of epidermis, so acute skin reactions are no longer always the limiting factor, although other acute effects, *e.g.* mucositis, may be. Denekamp (1973) has demonstrated experimentally how compensatory proliferation in skin or mucosa begins to accelerate at about 15 days after the beginning of treatments involving daily irradiation. Turesson and Notter (1984) have reinforced this finding clinically and have shown that repopulation in irradiated human skin enters an accelerated phase fairly abruptly after about 4 weeks of treatment. This is believed to be due to the stimulating effect of radiation-induced reproductive death, controlled by the rate of loss of sterilised cells. Thus, the amount of acute-tissue repopulation is governed largely by the overall time of a course of treatment. Turesson and Notter (1984) have also shown how more frequent fractionation leads to a probable redistribution of cells within the cell cycle, resulting in increased sensitisation.

In opting for MFD treatments, several key parameters are simultaneously altered and it is, therefore, difficult to predict with any certainty what the outcome on acute-responding tissues will be. If the MFD regime results in a reduction in the treatment time to a point where the accelerated proliferation observed in more conventional treatments cannot occur, acute-reactions are increased. This is often found to be the case clinically (see review by van der Scheuren et al, 1983), and has led to the introduction in some centres of split-course MFD techniques. Therefore too drastic a reduction in treatment time generally leads to an increase in the acute damage, but only the results of systematic clinical investigations will identify the nature of the interplay between the various parameters.

Thames et al (1983) and Fowler (1984b) have each shown that AF treatments tend to favour the case where tumour doubling times are relatively fast (*e.g.* a few days). This is because the reduced overall times of such treatments allow fewer tumour cell divisions, with a consequent reduction in the number of tumour cells which need to be killed. However, if the damage repair rates used above are representative, it is seen from the analysis that the likelihood of enhanced late-reactions rises as interfraction interval decreases. Whether or not such disadvantages would outweigh the potential advantages of enhanced tumour curability in a reduced treatment time would depend on the tumour proliferation rates involved.

Assuming once again that an AF regime is to be given which will give the same ERD to late-reacting tissues ($\alpha/\beta = 2.5$ Gy, $\mu = 0.46\ \text{h}^{-1}$) as a conventional regime giving 60 Gy in 30 daily fractions (ERD = 108 Gy) then, from Table I for three fractions/day, RE = 1.98. Therefore total dose to give = 108/1.98 = 54.5 Gy, *i.e.* approximately 27 fractions at 2 Gy/fraction

If the three fractions/day treatment is now to give the same ERD to tumour/early-reacting tissues ($\alpha/\beta = 10$ Gy, $\mu = 1.39\ \text{h}^{-1}$) as a conventional regime giving 60 Gy in 30 daily fractions (ERD = 72 Gy), the equivalent regime (at three fractions/day) is again found to be 60 Gy/30 fractions. Thus, the total dose required for matching of the late-effects is 5.5 Gy less (from 60 Gy to 54.5 Gy) than the total dose required for equivalent tumour effects.

If no treatment is given at weekends, to give 30 daily fractions requires an overall time of about 39 days; to give 27 fractions at three fractions/day requires an overall time of about 12 days. Is the reduction in tumour growth that is caused by reducing the treatment time by 27 days (from 39 days to 12 days) offset by the fact that 5.5 Gy less will have to be given if late reactions are not to be exceeded? To provide an answer to this it is necessary to consider possible tumour doubling times.

Thames et al (1984) have examined growth kinetics for some human solid tumours and have found that, with the exception of rapidly growing tumours such as Burkitt's lymphoma, the potential doubling times range upwards of 4 days. Assuming a working figure of 6 days, the reduction in treatment time considered above (27 days) will correspond to 4.5 tumour doubling times, *i.e.* a factor of $2^{4.5}$ (=23) fewer tumour cells would need to be killed in the AF treatment. If, very approximately, compensation for each tumour doubling requires about 3 Gy, then the dose in the AF treatment could be reduced by as much as 13.5 Gy (4.5 × 3 Gy), and the tumour kill effect would still be as high as in the 60 Gy/30 fractions case This dose reduction is much more than that required (5.5 Gy) to compensate for the diminished recovery of late-reacting tissues between the closely spaced fractions. On the basis of these figures there would, therefore, still appear to be a good case in favour of AF.

However, potential tumour doubling times are frequently very much less than volume doubling times, indicating large cell-loss factors (CLF) (Thames et al, 1983), and uncertainties in the CLF can lead to corresponding uncertainties in the doubling time estimates. In cases where potential doubling times are only a little longer than that considered above, the reduction in the tumour cell kill required in a reduced overall time may be relatively insignificant, thus requiring that the total AF dose cannot be reduced to any appreciable extent. In such instances, AF treatments would appear much less attractive, limited as they would be by the smaller repair of late-reacting tissues, and possibly also by enhanced acute reactions due to diminished opportunity for repopulation.

Where the tumour doubling time is known to be relatively long, the case for HF treatments, with the attendant advantages of smaller dose/fraction, is maintained (Table I).

Clearly the above indications could be of considerable significance, but it needs to be emphasised that such conclusions, particularly those relating to the potential limitations of AF treatments, would only be generally valid if the differential repair rates assumed here are true for all early- and late-reacting tissues. The specific values selected are those found in a relatively small sample of tissue types analysed by Thames (1984). It is important to bear in mind that it may subsequently be shown that μ values cannot be generalised, in which case specific values would be needed for each tissue in order to perform these calculations. Indeed, Ang et al (1985) have suggested that μ values may be further dependent on the magnitude of dose/fraction. Nevertheless, the influence on MFD treatments of differential repair rates between tissues has been previously predicted as being a possible limiting effect (Thames, 1984; Thames et al, 1984) and the LQ equations, which additionally accommodate the effects of differing α/β values and differing dose/fraction, do allow a more comprehensive analysis of the problem.

APPLICATION TO TBI TREATMENTS UTILISING A NUMBER OF SHORT FRACTIONS OVER A PERIOD OF HOURS

A number of authors (*e.g.* Cline et al, 1975) have reported TBI techniques involving the delivery of dose over a period of several hours, a frequent procedure being to give a number of small fractions during this period, rather than a truly continuous irradiation. The possible consequences of adopting this approach may be analysed by means of Equation (9).

Let:

$$Z = \frac{N(1-K^2)-2K(1-K^N)}{(1-K)^2}$$

i.e. that part of Equation (9) within the curly brackets. Then,

$$\text{RE} = 1+F_{\text{fract}}(\beta/\alpha)$$

where:

$$F_{\text{fract}} = (D_N/N)Z \qquad \text{(from Equation (9))}$$

Values of F_{fract} are plotted against N in Fig. 1 for two regimes: (A) assuming 10 Gy delivered in 6 h, (B) assuming 8 Gy delivered in 2 h.

In each case the results have been plotted for two values of repair constant; $\mu = 0.46\ \text{h}^{-1}$ and $\mu = 1.39\ \text{h}^{-1}$. The graph indicates also the value of F_{prot} ($\text{RE} = 1+(\beta/\alpha)F_{\text{prot}}$) expected if the regimes were truly protracted, calculated via Equation (Z). Clearly the behaviour of F_{fract} is complex, but the general conclusion to be drawn is that this parameter (and hence RE) is notably smaller in the fractionated case for tissues in which the damage repair is fairly rapid. The differences between F_{prot} and F_{fract} tend to become insignificant for fraction numbers >25.

It is intuitively obvious that, for increasing fraction numbers and smaller fraction intervals, the REs of such fractionated and protracted regimes should tend to the

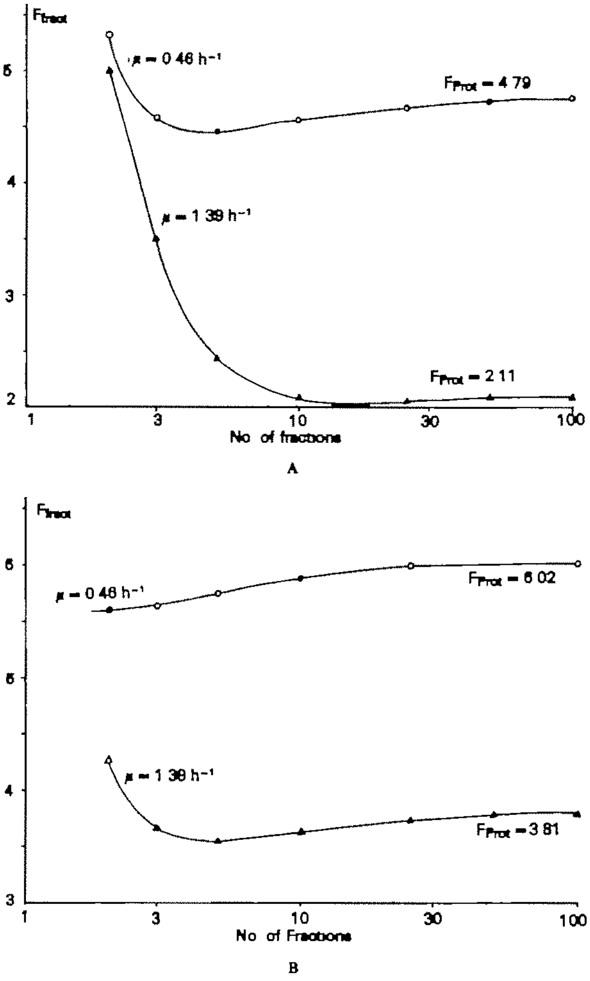

FIG 1

Behaviour of the parameter F_{fract} for two different fractionated treatment regimes and two values of repair constant. (A) 10 Gy given in 6 h. (B) 8 Gy given in 2 h.

same value. This is clear from the curves considered in Fig. 1, and is proved mathematically in Appendix II.

Multifractionated TBI treatments within the space of a few hours ought, therefore, to produce the same effects on all tissues as when the same total dose is given in a low dose-rate continuous irradiation in the same time period, *i.e.* when the average dose-rate is the same in each case. This conclusion is supported by the work of Lehnert (1985), commenting on the anomalous results of Kim et al (1985).

Before leaving this consideration of TBI, it may be of interest to re-examine one of the practical problems previously investigated (Examples D and E of Dale, 1985). It was found that there were clear theoretical advantages to be gained by delivering TBIs in a few acute fractions instead of with continuous irradiations given in a few hours, principally on account of the expected decrease in the incidence of lung reactions without loss of effect on the bone marrow. These conclusions were reached on the basis of *both* the critical tissues having a repair half-life of 1.5 h. Because of the possible faster repair rate associated with bone marrow (Thames et al (1984) have suggested a $T_{1/2}$ as low as 0.3 h), the case for fractionation may be even better than previously indicated. The calculations will therefore be repeated, this time using an assumed repair half-life of 0.5 h for the bone marrow.

Continuous irradiation: 10 Gy at an average dose-rate of 1.67 Gy h^{-1} over an extended time of 6 h. Lung and marrow doses identical.

Assume: bone marrow $\alpha/\beta = 15$ Gy; $T_{1/2} = 0.5$ h; $\mu = 1.39\ h^{-1}$, and lung $\alpha/\beta = 4$ Gy; $T_{1/2} = 1.5$ h; $\mu = 0.46\ h^{-1}$.

From Equation (C) of Dale (1985):
ERD (marrow) = 11.4 Gy and ERD (lung) = 22.0 Gy.

If the fractionated regime is to consist of five acute fractions, the dose/fraction (D_N) can be calculated from Equations (2) and (3) of this paper.

For bone marrow:

$$5D_N[1 + D_N/15] = 11.4\ \text{Gy}$$
$$i.e.\ D_N = 2.01\ \text{Gy}$$

For lung:

$$5D_N[1 + D_N/4] = 22.0\ \text{Gy}$$
$$i.e.\ D_N = 2.65\ \text{Gy}$$

Therefore, the same bone marrow depletion as in the protracted case can be obtained by 10.1 Gy (5 × 2.01 Gy) (fractionated). The same lung effect as in the protracted case would require 13.3 Gy (5 × 2.65 Gy) (fractionated). Thus, for the same degree of bone marrow damage, five acute fractions will "spare" the lung a dose of 3.2 Gy (*i.e.* 24%). This is a substantial improvement on the figure of 13% obtained by assuming similar repair half-lives (1.5 h) for both tissue types. Again, however, it must be stressed that precise values of these constants, as opposed to the generalisations used here, are important. Irrespective of this caution, the clinical case for fractionated TBI is now well established on account of the associated reduction in the incidence of pneumonitis (*e.g.* Pino et al, 1982).

DISCUSSION

In further developing the LQ theory from that previously presented, no new assumptions have been made, nor have any new parameters been introduced. The arguments advanced here are therefore no less valid than those which led to the development of equations giving the REs of fractionated, protracted and decaying source treatments. It is, however, important to understand that the clinical evidence to support the LQ approach is based almost entirely on studies in fractionated radiobiology. Iso-effect data from such studies, when plotted in the form of an F_e graph (Douglas & Fowler, 1975), behave in a way which is explainable if the underlying dose–response equation is indeed linear-quadratic in form. However, this is not an incontrovertible proof of the LQ theory. There may be other explanations as to why the data points behave in this particular manner; the apparent support for the LQ model may yet be coincidental.

The extended LQ model, although it provides further insights which appear logical, continues to rest on the assumption that the two-hit model provides a full explanation (at least for small to moderate doses/fraction) of underlying dose–effect curves. Fowler (1984b) has indicated other ways in which fractionated clinical data may be analysed, and Tucker (1984) has presented mathematical methods which do not merely derive estimates of α/β but, more importantly, are capable of rejecting data for which the calculation of an α/β ratio is unjustified. All these methods are important since, in the future, they may help in deciding whether to accept or reject the broad principles of the LQ theory.

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REFERENCES

ANG, K. K., XU, F.-X., LANDYUT, W. & VAN DER SCHEUREN, E., 1985. The kinetics and capacity of repair of sub-lethal damage in mouse lip mucosa during fractionated irradiations. *International Journal of Radiation Oncology, Biology, Physics, 11*, 1977–1983.

BARENDSEN, G. W., 1982. Dose fractionation, dose-rate and iso-effect relationships for normal tissue responses. *International Journal of Radiation Oncology, Biology, Physics, 8*, 1981–1997.

CHADWICK, K. H. & LEENHOUTS, H. P., 1973. A molecular theory of cell survival. *Physics in Medicine and Biology, 18*, 78–87.

CLINE, M. J., GALE, R. P. & STIEHM, E. R., 1975. Bone marrow transplantation in man. *Annals of Internal Medicine, 83*, 691–708.

DALE, R. G., 1985. The application of the linear-quadratic dose-effect equation to fractionated and protracted radiotherapy. *British Journal of Radiology, 58*, 515–528

—1986 Agreement of quadratic and CRE models in predicting the late effects of continuous low dose-rate radiotherapy—reply. *British Journal of Radiology, 59*, 194–195.

DENEKAMP, J, 1973. Changes in the rate of repopulation during multifraction irradiation of mouse skin. *British Journal of Radiology, 46*, 381–387.

DOUGLAS, B. G., 1982a. Implications of the quadratic cell survival curve and human skin radiation "tolerance doses" on fractionation and superfractionation dose selection. *International Journal of Radiation Oncology, Biology, Physics, 8*, 1135–1142.

—1982b. Superfractionation: its rationale and anticipated benefits *International Journal of Radiation Oncology, Biology, Physics, 8*, 1143–1153.

DOUGLAS, B G. & FOWLER, J. F, 1975. Fractionation schedules and a quadratic dose-effect relationship *British Journal of Radiology, 48*, 502–504.

FOWLER, J. F., 1984a What next in fractionated radiotherapy? *British Journal of Cancer, 49, Supp. 6*, 285–300

—1984b. Review: Total doses in fractionated radiotherapy. *International Journal of Radiation Biology, 46*, 103–120.

HENDRY, J. H & MOORE, J. V, 1985. Deriving absolute values of alpha and beta for dose fractionation. *British Journal of Radiology, 58*, 885–890

KIM, T. H., RYBKA, W. B, LEHNERT, S, PODGORSAK, E B. & FREEMAN, C. R, 1985. Interstitial pneumonitis following total body irradiation for bone marrow transplantation using two different dose rates *International Journal of Radiation Oncology, Biology, Physics, 11*, 1285–1291.

LEHNERT, S, 1985. Response of the lung to intermittent irradiation: the importance of average versus instantaneous dose rates. *International Journal of Radiation Oncology, Biology, Physics, 11*, 2183–2184.

LIVERSAGE, W. E., 1969a A general formula for equating protracted and acute regimes of radiation. *British Journal of Radiology, 39*, 338–349.

—1969b. The rate of decay of the dose equivalent of radiation induced sub-lethal damage, *Cell and Tissue Kinetics, 2*, 269–276.

—1971. A critical look at the ret. *British Journal of Radiology, 44*, 91–100.

MICHALOWSKI, A S., 1984. A critical appraisal of clonogenic survival assays in the evaluation of radiation damage to normal tissues. *Radiotherapy and Oncology, 1*, 241–246

O'DONOGHUE, J., 1986. Agreement of quadratic and CRE models in predicting the late effects of continuous low dose-rate radiotherapy. *British Journal of Radiology, 59*, 193.

PINO Y TORRES, J. L, BROSS, D. S, LAM, W-C., WHARAM, M. D., SANTOS, G. W. & ORDER, S. E, 1982 Risk factors in interstitial pneumonitis following allogenic bone marrow transplantation. *International Journal of Radiation Oncology, Biology, Physics, 8*, 1301–1307.

ROESCH, W C., 1978 *Third Symposium on Neutron Dosimetry in Biology and Medicine* Ed. by G. Burger & H. G. Ebert, (Commission of the European Communities, Luxembourg), p.1.

THAMES, H. D., 1984. Effect-independent measures of tissue responses to fractionated irradiation. *International Journal of Radiation Biology, 45*, 1–10.

—1985. An "incomplete-repair" model for survival after fractionated and continuous irradiations. *International Journal of Radiation Biology, 47*, 319–339.

THAMES, H. D., PETERS, L. J., WITHERS, H. R & FLETCHER, G H, 1983. Accelerated fractionation vs hyperfractionation: rationales for several treatments per day. *International Journal of Radiation Oncology, Biology, Physics, 9*, 127–138.

THAMES, H. D., WITHERS, H. R. & PETERS, L. J., 1984. Tissue repair capacity and repair kinetics deduced from multifractionated or continuous irradiation regimes with incomplete repair. *British Journal of Cancer, 49*, 263–269.

THAMES, H D., WITHERS, H. R., PETERS, L J & FLETCHER, G J., 1982. Changes in early and late radiation responses with altered fractionation: implications for dose-survival relationships *International Journal of Radiation Oncology, Biology, Physics, 8*, 219–226.

TUCKER, S. L, 1984. Tests for the fit of the linear-quadratic model to radiation iso-effect data *International Journal of Radiation Oncology, Biology, Physics, 10*, 1933–1939.

TURESSON, I. & NOTTER, G, 1984. The influence of the overall treatment time in radiotherapy on the acute reaction. comparison of the effects of daily and twice-a-week fractionation on human skin. *International Journal of Radiation Oncology, Biology, Physics, 10*, 607–618.

VAN DER SCHEUREN, E., VAN DEN BOGAERT, W. & ANG, K K., 1983. In *The Radiobiological Basis of Radiotherapy*. Ed. by G G. Steel, G. E Adams & M. J Peckham (Elsevier, Amsterdam)

WILLIAMS, M. V., DENEKAMP, J & FOWLER, J. F., 1985. A review of α/β ratios for experimental tumours. *International Journal of Radiation Oncology, Biology, Physics, 11*, 87–96.

APPENDIX I

Equation (7) is

Total Type B damage in N fractions

$$= \beta D_N^2 \left\{ N + 2 \sum_{i=1}^{N-1} (N-i) \exp(-i\mu x) \right\}$$

Let

$$S = \sum_{i=1}^{N-1} (N-i) K^i$$

Where

$$K = \exp(-\mu x)$$

$$S = (N-1)K + (N-2)K^2 + (N-3)K^3 + \ldots + K^{N-1}$$

$$KS = (N-1)K^2 + (N-2)K^3 + \ldots + K^N$$

Therefore

$$S(1-K) = (N-1)K - (K^2 + K^3 + \ldots + K^N) \qquad \text{(X)}$$

Let

$$Q = K^2 + K^3 + \ldots + K^N$$

$$KQ = K^3 + \ldots + K^{N+1}.$$

Therefore:

$$Q(1-K) = K^2 - K^{N+1}$$

i e

$$Q = \frac{K^2 - K^{N+1}}{1-K} \qquad \text{(Y)}$$

Substituting (Y) into (X):

$$S(1-K) = (N-1)K - \frac{K^2 - K^{N+1}}{1-K}$$

i.e

$$S = \frac{K(N-1) - K^2 N + K^{N+1}}{(1-K)^2}$$

Substituting S back into Equation (7) and simplifying we have:

Total Type B damage in N fractions

$$= \beta D_{\mathrm{N}}^{2}\left\{\frac{N(1-K^{2})-2K(1-K^{N})}{(1-K)^{2}}\right\}$$

APPENDIX II

From Appendix I,
Total Type B damage in fractionated irradiation

$$= \beta D_{\mathrm{N}}^{2}\left\{\frac{N(1-K^{2})-2K(1-K^{N})}{(1-K)^{2}}\right\}$$

since $K = \mathrm{e}^{-\mu x}$

Total treatment time, $T = (N-1)x$

i.e. $T \doteq Nx$ for large N

Therefore the expression for Type B damage becomes:

$$\beta D_{\mathrm{N}}^{2}\left\{\frac{N(1-\mathrm{e}^{-2\mu x})-2\mathrm{e}^{-\mu x}(1-\mathrm{e}^{-\mu T})}{(1-\mathrm{e}^{-\mu x})^{2}}\right\}$$

$$= \beta D_{\mathrm{N}}^{2}\left\{\frac{N(1+e^{-\mu x})}{(1-\mathrm{e}^{-\mu x})} - \frac{2\mathrm{e}^{-\mu x}(1-\mathrm{e}^{-\mu T})}{(1-\mathrm{e}^{-\mu x})^{2}}\right\}$$

For decreasing fraction intervals $x \rightarrow 0$ and $\mathrm{e}^{-\mu x} \rightarrow 1$.

Therefore Type B damage

$$\rightarrow \beta D_{\mathrm{N}}^{2}\left\{\frac{2N}{(1-\mathrm{e}^{-\mu x})} - \frac{2(1-\mathrm{e}^{-\mu T})}{(1-\mathrm{e}^{-\mu x})^{2}}\right\}$$

$$\rightarrow \beta D_{\mathrm{N}}^{2}\left\{\frac{2N(1-\mathrm{e}^{-\mu x})-2(1-\mathrm{e}^{-\mu T})}{(1-\mathrm{e}^{-\mu x})^{2}}\right\}$$

$$\rightarrow \beta D_{\mathrm{N}}^{2}\left\{\frac{2N(\mu x - \ldots)-2(1-\mathrm{e}^{-\mu T})}{(\mu x^{2} - \ldots)}\right\}$$

Doses in fractionated and protracted cases are to be equal, therefore $ND_{\mathrm{N}} = RT$ where R is the protracted dose-rate.

Therefore Type B damage

$$\rightarrow \beta\frac{R^{2}T^{2}}{N^{2}}\left\{\frac{2\mu T-2(1-\mathrm{e}^{-\mu T})}{(\mu T^{2}/N^{2})}\right\}$$

$$\rightarrow 2\beta R^{2}\left\{\frac{T}{\mu} - \frac{1-\mathrm{e}^{-\mu T}}{\mu^{2}}\right\}$$

$$\rightarrow \frac{2\beta R^{2}}{\mu}\left\{T - \frac{1}{\mu}[1-\mathrm{e}^{-\mu T}]\right\}$$

This is the expression for Type B damage in protracted irradiation given by Dale (1985).

Type A damage in N fractions $= N\alpha D_{\mathrm{N}} = \alpha RT$

Therefore, using Equation (5),

$$\mathrm{RE} = 1 + \frac{2R}{\mu}\left(\frac{\beta}{\alpha}\right)\left\{1 - \frac{1}{\mu T}[1-\mathrm{e}^{-\mu T}]\right\} \qquad \text{(Z)}$$

which is the expression for $\mathrm{RE}_{\mathrm{prot}}$ given by Dale (1985). Thus, $\mathrm{RE}_{\mathrm{Fract}} \rightarrow \mathrm{RE}_{\mathrm{Prot}}$.

Book reviews

Hyperthermia. Ed. by D. J. Watmough and W. M. Ross, pp. vii+242+index, 1986 (The Blackie Publishing Group, Glasgow), £35.00.

This book is 245 pages long and is divided into 10 chapters, each contributed by different authors. The areas covered are the effects of heat alone or combined with drugs, thermotolerance, heating methods, experience with whole-body heating, temperature measurement and prediction, and a survey of commercial equipment.

An obvious gap is the lack of information on the use of hyperthermia and ionising radiation. This omission really precludes the use of this book as a general working text on hyperthermia, certainly for radiotherapists Ultrasonic heating maintains a high profile throughout the book, obviously reflecting the special interests of the contributors and editors. However, this does not accurately represent the current dominant use of electromagnetic heating techniques in hyperthermia research and clinical use.

On the positive side, I found the chapter on hyperthermia and drugs to be a comprehensive summary, with 200 papers referenced. The chapter by Law and Pettigrew contains an interesting description of their experience with the use of molten wax for whole-body heating, although this technique is now rarely used. Sciandra and Gerweck provide an excellent discussion on some proposed models for thermotolerance

Overall, I found this book disappointing It does not provide a comprehensive overview of hyperthermia as intended, although it must be said that such a task is by now almost impossible in such an extensive field of research. Several of the individual contributions, however, provide useful sources of information, particularly for those interested in ultrasound.

M. Joiner

Magnetic Resonance Imaging (Principles and Applications). By David Kean and Michael Smith, pp. viii+161+index, 1986 (William Heinemann Medical Books Ltd, London), £27.50. ISBN 0-433-18265-2

The stated aim of this book is to introduce both the physical and clinical applications of magnetic resonance imaging. The authors are a radiologist and physicist with wide experience of using a low-field resistive imaging instrument.

The first half of the book is a lucid, non-mathematical description of the physics and technical aspects. The clinical applications are grouped in anatomical areas with approximately half the images from the Edinburgh unit, the remainder being supplied by Hammersmith, Nottingham, Cleveland Clinic and University of California San Francisco. Image quality is variable but the relevant abnormalities are clearly demonstrated.

An introduction to a complex subject which crosses different spheres of interest is very difficult, but the authors have succeeded. The publishers and printers should also be congratulated on the outstanding presentation of the text, illustrations and images

Anyone wanting an introduction to magnetic resonance imaging will find this book valuable.

C. E. L. Freer

1986, *The British Journal of Radiology*, 59, 929–930 SEPTEMBER 1986

Technical notes

A technique for delivering uniform dose at the junction of two spinal fields

By *Andrew Wu, Ph.D., E. S. Sternick, Ph.D., †S. Shahabi, Ph.D. and R. D. Zwicker, Ph.D.

Medical Physics Division, Department of Therapeutic Radiology, Tufts–New England Medical Center,
171 Harrison Avenue, Boston, Massachusetts 02111, USA

(*Received February 1986*)

In the treatment of medulloblastoma and other malignant tumours of the central nervous system, often the entire spine must be irradiated as well as the cranial contents (Paterson & Farr, 1953; Bloom et al, 1969; Jenkin, 1969; Bloom, 1971). Because of the length of the spinal axis, it is sometimes necessary to use two abutting fields in order to include the whole spinal cord in the treatment field. We report here the use of a simple wedge technique to provide a uniform dose at the spinal-field junction. Similar approaches to ensure dose uniformity across the junctions of the multiple fields used during total lymphoid irradiation of Hodgkin's disease have been described previously by others (Armstrong & Tait, 1973; Griffin et al, 1976; Fraass et al, 1983; Doppke, 1983).

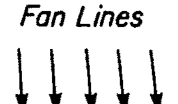

FIG. 1.
Schematic design of the J-shaped junction wedge or "J wedge".

The simple design of this J-shaped junction wedge ("J wedge") is shown in Fig. 1. Approximately 5 cm thick and 3 cm wide, the J wedge was cast from a low melting point lead alloy and mounted on plexiglass. It fits into the standard wedge slot of the Varian Clinac 4/100 linear accelerator without interfering with the blocks or blocking tray. An important and distinct feature of the J wedge is that it is mounted with the thick edge downward so that the position of the light field on the wedge can be clearly seen. As long as the edge of the X-ray beam is in alignment with the top of the wedge, any variation in the size of the treatment fields results in very small changes in the length of the beam path traversing the wedge. Consequently, the same J wedge can be used for different field sizes.

The technique for using the wedge is illustrated in Fig. 2. First, the edge of one open field is marked on the patient's skin (a'). Next, the wedge is positioned at the abutting edge so that the edge of the light field is aligned along the top of the wedge and the projected shadow is marked on the skin (a). For the adjacent

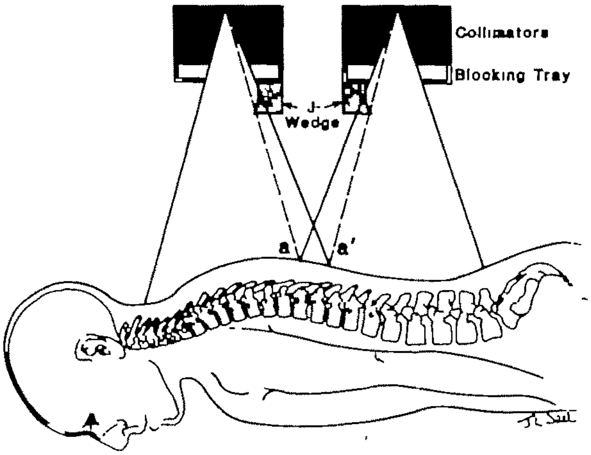

FIG. 2.
Schematic illustration of the clinical set-up using the wedge.

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*Author for reprints.

†Supported by NCI Award (#5T32-CA-09045). Present address: Division of Clinical Cancer Center, Madison, WI 53792, USA.

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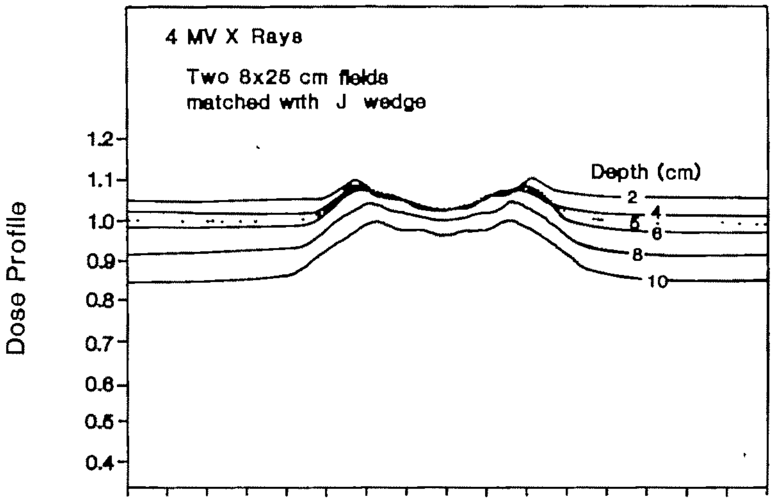

FIG. 3.

Plot of dose profiles, normalised to the dose prescribed at 5 cm depth, across the junction of two 8 cm × 25 cm fields matched with the J wedge at various depths for 4 MV X rays. The dotted line is the profile at the nominal depth of the spinal axis, 5 cm.

field, the open field edge is simply matched to the shadow line, a, on the first field and the wedge is positioned as before, but in reverse position to match a. Dose profiles taken in a phantom for two adjacent 8 cm × 25 cm fields with the J wedge in place show only small variations at the junction region at depths ranging from 2 cm to 10 cm (Fig. 3).

In summary, the J wedge provides a spinal cord abutment technique which generates dose uniformity at the field junction, reduces dose variation resulting from clinical set-up error and allows simplicity and efficiency in everyday use.

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REFERENCES

ARMSTRONG, D. & TAIT, J., 1973. The matching of adjacent fields in radiotherapy. *Radiology*, *108*, 419–422.

BLOOM, H. J. G., 1971. Concepts in the natural history and treatment of medulloblastoma in children: increasing survival rates and possible risks with current radiotherapy techniques. *CRC Critical Reviews in Radiological Sciences*, *2*, 89–143.

BLOOM, H. J. G., WALLACE, E. N. K. & HENK, J. M., 1969. The treatment and prognosis of medulloblastoma in children. *American Journal of Roentgenology*, *105*, 43–62.

DOPPKE, K., 1983. Treatment strategies—Hodgkin's disease. In *Advances in Radiation Therapy Treatment Planning*. Ed by A. E. Wright & A. L. Boyer (AIP, New York), pp. 341–355.

FRAASS, B. A., TEPPER, J. E., GLATSTEIN, E. & VAN DE GEIJN, J., 1983. Clinical use of a match-line wedge for adjacent megavoltage radiation field matching. *International Journal of Radiation Oncology, Biology, Physics*, *9*, 209–216.

GRIFFIN, T. W., SCHUMACHER, D. & BERRY, H. C., 1976. A technique for cranial-spinal irradiation. *British Journal of Radiology*, *49*, 887–888.

JENKIN, R. D. T., 1969. Medulloblastoma in childhood: radiation therapy. *Canadian Medical Association Journal*, *100*, 51–53.

PATERSON, E. & FARR, R. F., 1953. Cerebellar medulloblastoma: treatment by irradiation of the whole central nervous system. *Acta Radiologica*, *39*, 323–336.

An improved system of customised photon shielding for radiotherapy

By G. R. Plant, D. Challoner and D. A. L. Morgan

Departments of Medical Physics and Radiotherapy, General Hospital, Nottingham NG1 6HA

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Modern radiotherapy requires accurate customised beam shielding. It has been shown (Griffiths & Pearcey, 1985) that shielding blocks rigidly and precisely attached to the head of the treatment machine are the best way of achieving this. These blocks are usually produced by tracing the desired outline on a planning radiograph, and translating this geometrically to a styrene block, cut out correspondingly by a hot wire (Jones, 1971). A dense shielding medium is then poured into the cut-out spaces.

Problems have always been present in conventional designs of hot-wire cutter. The height of the cutting frame necessary to simulate focus-to-film distances (FFDs) in extended focus-to-skin-distance (FSD) treatments is often greater than normal ceiling height, particularly if a comfortable bench height is allowed for the operator. Also, on early cutters, the hot wire formed a section of flexible line from the focus/pivot to the film, and variation in length was accommodated by a spring or counterbalance (Edland & Hansen, 1969; Powers et al, 1973). Drag on the line during the cutting operation of this type of jig can cause gross errors in the styrene cut-out outline, particularly at extended FSDs (Paliwal & Asp, 1976). Attempts have been made (Sorensen & Goshaw, 1975) to minimise this effect by the use of a rigid cutting frame suspended from the pivot and incorporating a telescopic tracing stylus. The addition of a counterbalance above the pivot is a further modification, attempting to reduce the force required at the stylus and the consequent bending moment on the cutting frame. Although an improvement, this still allows errors in the cut outline, and again increases the height and complexity of the jig. Other solutions have in some way involved minifying the template or film to be traced, so reducing the tracer length below the styrene block. Tray shift techniques are generally complicated procedures despite the claim of simplicity (Douglas et al, 1984) and may introduce errors of divergence (Nair & Sadeghi, 1980). Scaled down outlines, for example by computer (de Vos, 1982), can be expensive and time-consuming procedures, introducing another level (scaling) at which errors may occur.

Our solution to these problems has been to remove completely the hot-wire suspension from between the styrene block level and the film. This section is replaced by a variable-ratio pantograph (Fig. 1), so converting the vertical geometry of this section to horizontal. The main problems in more conventional cutting jigs are thus overcome. Firstly, the complete unit is contained on a bench-top at normal working height (Fig. 2). The area used is about 100 cm × 150 cm and the maximum height from bench to pivot is 100 cm. Secondly, due to the rigidity of the pantograph main support bearing, considerable tension can be put on the cutter wire, so minimising drag at normal tracing speeds. Focus-to-shielding tray distances may be set to any position between the focus/pivot and the pre-determined pantograph cutter-wire attachment point. A single gauge, calibrated directly in FFDs, is used to make three necessary arm-length adjustments on the pantograph, and a transparent cursor moves freely over the film to trace shielding lines.

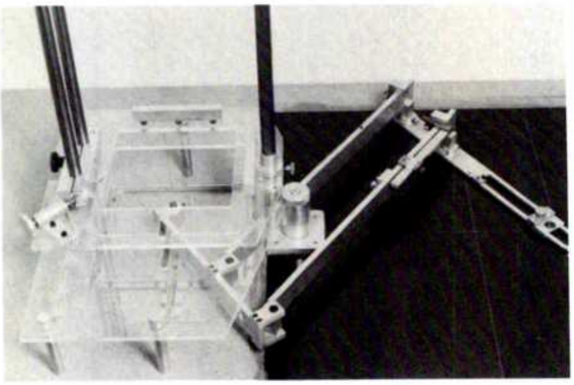

FIG. 1.
Close-up pantograph mechanism.

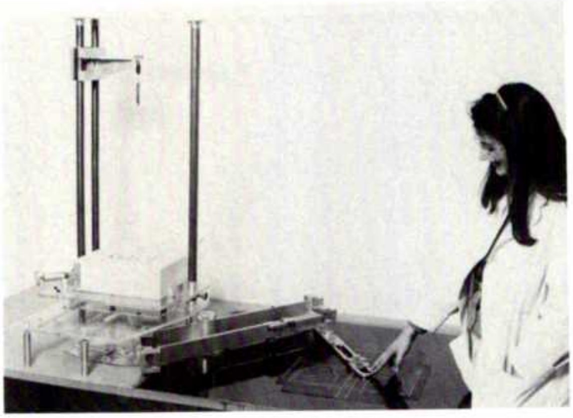

FIG. 2.
New jig.

The localisation film has lines applied in white wax pencil to give clarity without the necessity of a light box (although one could easily be incorporated in the table). The film is simply taped to the table with the field centre located under the cursor of the pantograph (previously set to the correct FFD and positioned at the central axis of the jig). A detent is provided for the central axis position. After setting the film the pantograph arm is moved to a position allowing insertion of the styrene block, which is located using one corner only as reference and clamped in the tray position. The corner reference is subsequently used in positioning the block for checking and casting.

The styrene mould is taped to prevent alloy leakage and clamped to the casting base. The datum corner locates on two vertical edges. Screws are inserted from below through the most appropriate holes in the casting base to pierce the tape and protrude into the mould cavities (Fig. 3). New holes are drilled when required. The casting base and mould are positioned on the cooling plate before being filled with low-melting-point alloy. A major difficulty we encountered was in controlling the cooling rate of the alloy; if this is not achieved, shrinkage voids occur, and X-ray transmission through the blocks increases. By regulating hot and cold water circulation through the cooling plate, the development of such voids is prevented. On setting, the alloy blocks are retrieved by

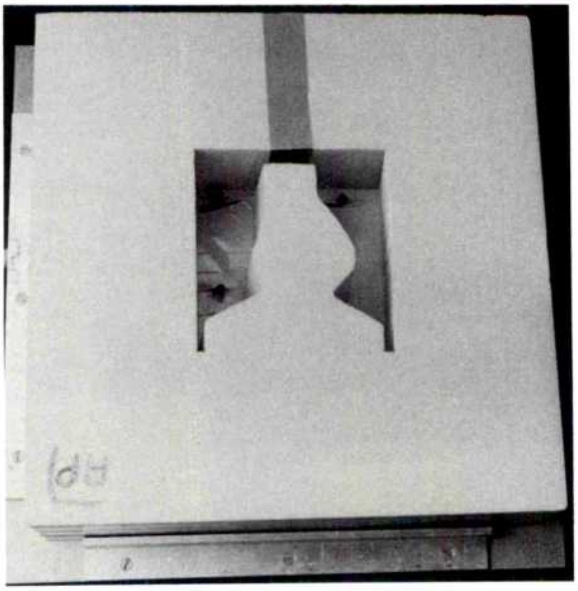

FIG. 3.

Styrene cut-out and casting base with screws in voids.

removing the screws and breaking away the styrene. The threaded holes remaining in the blocks enable fixing to a shadow tray ready for use on the treatment set.

Shadow trays are standard and interchangeable on the Department's three linear accelerators, although mounting arrangements vary to accommodate different focus-to-mounting-ring distances. Holes on the shadow tray are jig drilled from the casting base by locating the tray accurately to the underside of the base.

Alignment checks may be made at the styrene cut-out and the finished shadow tray stages. There is a risk of introducing alignment errors in simulating treatment set optical systems, and it has proven more accurate to make these checks on the treatment set for which the shield is intended, although a simple separate optical jig is available for convenience.

The styrene cut-out is positioned on an adapted tray carrier, again using the datum corner for location, and the projected beam-defining light observed for coincidence with the original film shielding lines. True divergence is checked by applying a pointed instrument to the sides of the cut-out and observing the shadows cast. At the later stage a similar procedure is carried out but with the completed shielding tray in its head mounting attachment.

The complete shielding system has now been in use for over 2 years. It has completely fulfilled the original requirements and has produced some unforeseen benefits. Due to the high accuracy and predictable operation of the hot-wire cutter, the alignment check on the styrene cut-out is now omitted and checks on the finished trays only are necessary. Errors in shielding outline are consistently within 0.5 mm of the original film outline and divergency errors are undetectable. These improvements are entirely due to the construction of the cutting jig allowing a rigidly supported, comparatively taut hot wire, and the ease of movement in the pantograph which allows the operator to trace the outline accurately and smoothly.

The range of FFDs could be extended considerably without the cutting jig becoming unwieldy, although in this unit a maximum distance of 175 cm has been found adequate.

Styrene blocks of accurate dimensions and squareness are often difficult to purchase or produce. The use of a datum corner only for location during the process simplifies the production of the block which requires only two sides to be vertical and mutually normal. The remaining shape is not critical beyond the required shielding areas.

The advantages of using solidly mounted blocks have been realised and the range of applications is being extended. The technique is now being applied to multiple-field head and neck treatments, where varying gantry angles are set.

REFERENCES

DOUGLAS, K., WILSON, W. P., & BRIDGE, L. R., 1984. A simple shift technique for the production of shielding blocks at extended treating distances. *British Journal of Radiology*, *57*, 273.

EDLAND, R. W. & HANSEN, H., 1969. Irregular field-shaping for ^{60}Co teletherapy. *Radiology*, *92*, 1567–1569.

GRIFFITHS, S. E. & PEARCEY, R. G., 1985. The reproducibility of large lead protected radiotherapy fields to the abdomen and pelvis. *Radiography*, *51*, 247–250.

JONES, D., 1971. A method for the accurate manufacture of lead shields. *British Journal of Radiology*, *44*, 398–399.

NAIR, T. K. M. & SADEGHI, A., 1980. Simulation of extended mantle field by tray shift technique. *British Journal of Radiology*, *53*, 1088–1089.

PALIWAL, B. R., & ASP, L., 1976. A technique to evaluate styrofoam cutouts used in irregular field shaping. *International Journal of Radiation Oncology, Biology, Physics*, *1*, 791–793.

POWERS, W. E., KINZIE, J. J., DEMIDECKI, A. J., BRADFIELD, J. S. & FELDMAN, A., 1973. A new system of field shaping for external beam radiation therapy. *Radiology*, *108*, 407–411.

SORENSEN, A. & GOSHAW, L., 1975. Simple design for a stryofoam cutter. *Medical Physics*, *2*, 338–339.

VOS, R. J. DE, 1982. A compact hot-wire cutting system. *British Journal of Radiology*, *55*, 315–316.

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Case reports

Computed tomography and sonography of cystic adventitial disease

By T. P. Fitzjohn, F.R.C.R., *F. E. White, M.R.C.P., F.R.C.R., H. W. Loose, F.R.C.R. and †G. Proud, F.R.C.S.

Departments of Radiology and †Surgery, Freeman Hospital, Freeman Road, Newcastle upon Tyne NE7 7DZ

(*Received November 1985*)

Cystic adventitial disease (CAD) is an uncommon but important disorder, mainly of the vascular system. Usually, a single macroscopic mucin-containing cyst develops in a focal collection of microscopic cysts within the adventitia of a vessel, most commonly the popliteal artery. This disorder of unknown aetiology has a strong male predominance (8 : 1 male : female ratio) and usually affects relatively young patients (mean age 42 years) who, therefore, present with intermittent claudication at an age younger than expected for degenerative arterial disease (Flanigan et al, 1979).

Distinction from other causes of intermittent claudication, and in particular atheroma, is important as the prognosis of CAD is good and its treatment may differ.

The typical angiographic appearances have previously been described (Schlesinger & Gottesman, 1976). During the preparation of this paper, two reports of the appearances on computed tomography (CT) and ultrasound have been published (Deutsch et al, 1985; Wilbur et al, 1985) and we wish to report a further case with similar findings.

CASE REPORT

An essentially fit 49-year-old man presented with a 6-month history of left calf claudication (march tolerance 100 m). The patient was a non-smoker, of near average weight, with successfully treated mild hypertension. There was no history of local trauma. On palpation the left popliteal pulse was markedly diminished and the ipsilateral distal pulses absent, otherwise the physical examination and in particular, the rest of the cardiovascular system was normal. A full relevant laboratory screen was normal.

A transfemoral aortogram revealed a smooth extrinsic impression on the proximal left popliteal artery (Fig. 1). There was no post-stenotic dilatation or atheroma, and good distal run-off was shown. The appearances were consistent with CAD; ultrasound and CT were employed to confirm this.

Sonography of the popliteal fossa (Toshiba Sonolayer, 3.5 mHz linear-array probe) in longitudinal and transverse planes showed a longitudinally orientated convex lesion of the antero-lateral arterial wall. There was a uniform coarse granular echo-pattern consistent with homogeneous soft tissue or viscid fluid (Fig. 2).

Computed tomography of the popliteal fossa (Picker 1200SX), before and during an intravenous contrast bolus of Urografin 310 (meglumine diatrizoate, Schering) showed a lesion, 4 cm long and 1.3 cm in diameter, arising in the arterial wall. Contrast-medium administration was needed to show the severely compressed arterial lumen (Fig. 3). The attenuation at the centre of the lesion was 25 HU and did not enhance, but at the periphery it increased from 30 HU to 50 HU. The origins of the paired superior geniculate arteries could be seen to be affected in the process.

At surgery, a typical lesion of CAD with the predicted

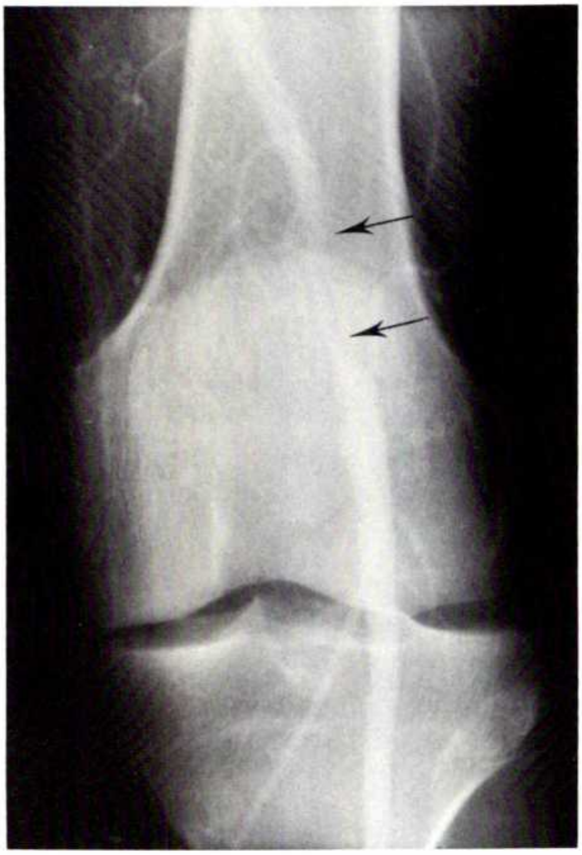

FIG. 1.

Arteriogram showing a 5 cm stenosis of the proximal popliteal artery (arrows). This is smooth, eccentric and with no post-stenotic dilatation or atheroma. There is no significant collateral circulation. Typical features of CAD.

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*Author for correspondence.

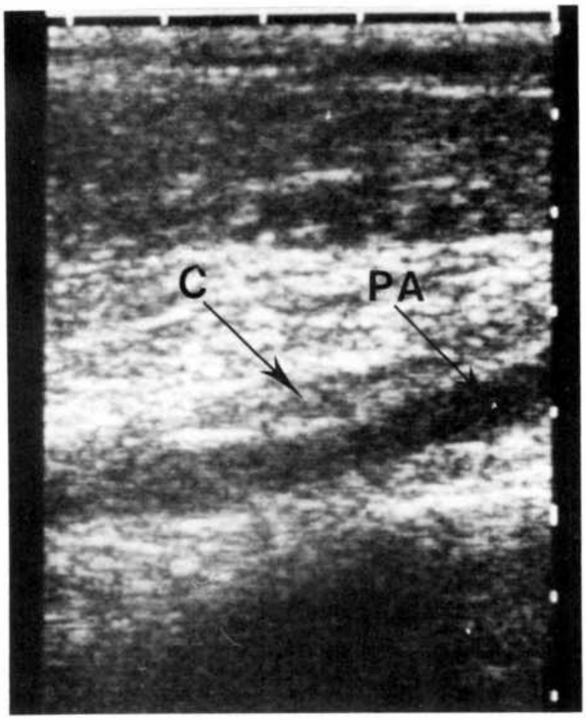

FIG. 2.

Longitudinal ultrasound scan showing a 5 cm × 1 cm biconvex lesion (C), in the antero-lateral wall of the popliteal artery (PA). Uniform coarse granular echo-pattern. (The degree of luminal stenosis was underestimated due to the obliquity of the scan plane.)

morphology was found. Due to the advanced state of the lesion with intimal damage, it was excised and a reverse venous homograft inserted (Fig. 4). Good distal flow was restored with relief of the intermittent claudication.

Pathological examination revealed a single macroscopic mucin-containing cyst in a bed of adventitial myxoid cystic degeneration. There was subintimal dissection due to turbulent flow but no atheroma was found.

DISCUSSION

The incidence of cystic adventitial disease has been reported as one per 1200 cases of intermittent calf claudication (Hamming & Vink, 1965) but its true incidence may be higher, some lesions being bypassed without direct inspection, on the assumption of an atheromatous aetiology.

It is important to make the diagnosis of CAD prior to surgical intervention as the treatment of early disease is by cyst aspiration or deroofing. Cyst aspiration has traditionally been performed through an open incision in the calf but CT-guided aspiration has been reported (Deutsch et al, 1985) and ultrasound-guided aspiration should also be technically feasible. Ten per cent, however, may recur, when the above procedures can be repeated or excision performed. The prognosis of CAD is good compared with atheromatous disease, as the lesion is usually solitary.

Imaging of CAD is usually confined to femoral arteriography. The characteristic feature of the stenotic form is extrinsic smooth compression of the contrast column which may extend to surround it. There is usually no post-stenotic dilatation or atheroma, but eventually turbulence will lead to intimal damage, thrombus formation and total occlusion.

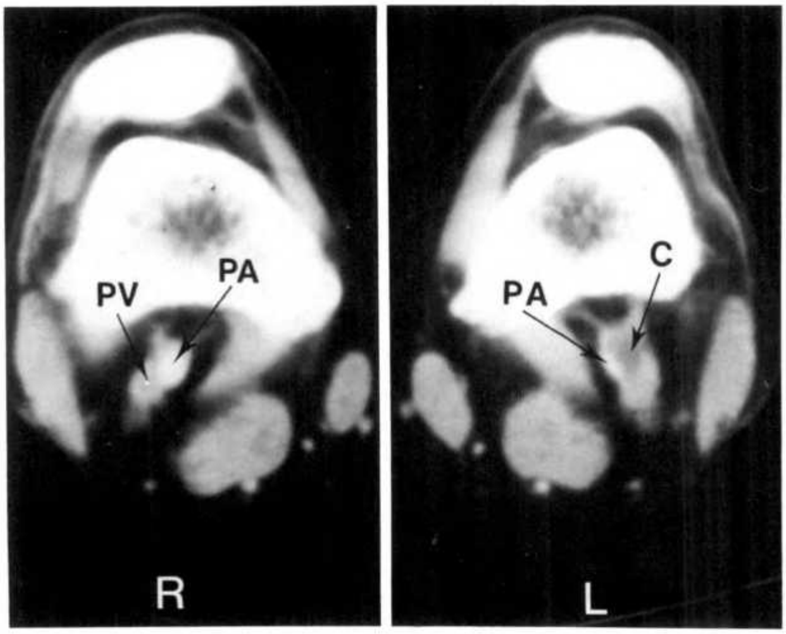

FIG. 3.

Axial CT showing both popliteal fossae. The normal right popliteal artery (PA) and vein (PV) are clearly shown. The left arterial lumen (PA) is compressed by the cyst (C).

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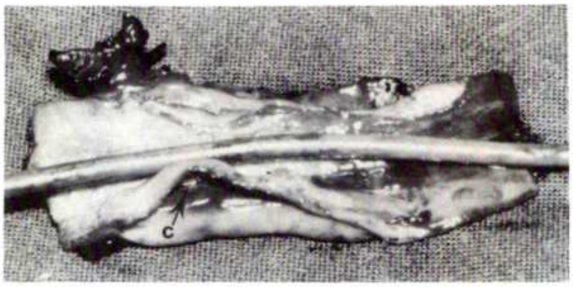

FIG. 4.

Excised specimen: incised and laid open longitudinally. A Ryle's tube has been placed along the lumen. The cyst (C) is seen in the arterial wall.

Angiographically, the differential diagnosis of stenotic CAD is the extrinsic compressive lesions of thrombosed popliteal artery aneurysms, entrapment syndromes, Baker's cysts and also atypical non-ulcerating atheroma. Computed tomography and ultrasound are valuable in differentiating the above from CAD.

This is the second reported case of CAD where both CT and ultrasound have been employed in the pre-surgical diagnosis and the close similarity of imaging findings would suggest that the above features may be typical of this condition; either imaging modality may have therapeutic implications.

We recommend ultrasound and CT of the popliteal fossa in cases of intermittent claudication when angiography suggests an extrinsic cause (particularly in the higher-risk group for CAD of relatively young men), firstly to establish the presence of a disease of lower morbidity and mortality and secondly as a possible aid to therapy.

REFERENCES

DEUTSCH, A. L., HYDE, J., MILLER, S. M., DIAMOND, G. G. & SCHANCHE, A. F., 1985. Cystic adventitial degeneration of the popliteal artery: CT demonstration and directed percutaneous therapy. *American Journal of Roentgenology*, *145*, 117–118.

FLANIGAN, D. P., BURNHAM, S. J., GOODREAU, J. J. & BERGAN, J. J., 1979. Summary of cases of adventitial cystic disease of the popliteal artery. *Annals of Surgery*, *189*, 165–175.

HAMMING, J. J. & VINK, M., 1965. Obstruction of the popliteal artery at an early age. *Journal of Cardiovascular Surgery*, *6*, 516–524.

SCHLESINGER, A. & GOTTESMAN, L., 1976. Cystic degeneration of the popliteal artery. *American Journal of Roentgenology*, *127*, 1043–1045.

WILBUR, A. C., WOELFEL, G. F., MEYER, J. P., FLANIGAN, D. P. & SPIGOS, D., 1985. Adventitial cystic disease of the popliteal artery. *Radiology*, *155*, 63–64.

Pneumoretroperitoneum following iliac crest trephine

By *M. P. Williams, M.A., F.R.C.R. and †G. A. Ford, M.A., M.R.C.P.

Departments of Radiology and †Radiotherapy, Addenbrooke's Hospital, Hills Road, Cambridge CB2 2QQ

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Gas within the retroperitoneum is usually a sign of serious gastrointestinal or urinary tract pathology. Most commonly, it results from bowel perforation secondary to inflammatory or ulcerative disease, blunt or penetrating trauma or to iatrogenic manipulation such as double-contrast barium enema or colonoscopy (Lezak & Goldhammer, 1974; Peterson et al, 1982). Retroperitoneal gas may also result from pancreatitis complicated by bacterial infection or infection in the perirenal space (Meyers, 1974). It has also been reported as a complication of mechanical ventilation when, following alveolar rupture, air tracks into the mediastinum and then passes retrocrurally into the retroperitoneum (Powner et al, 1976). We wish to report a case of pneumoretroperitoneum demonstrated by computed tomography (CT) which we believe to be the first case reported as a complication of iliac crest trephine.

CASE REPORT

A 54-year-old woman presented with a left axillary mass. She was otherwise well, with no symptoms. Clinical examination revealed left axillary lymphadenopathy but no other abnormal physical findings. An excision biopsy of the left axillary nodes was performed. Histology showed a diffuse centroblastic, centrocytic non-Hodgkin's lymphoma. As part of the staging procedure for her lymphoma the patient had a bone marrow biopsy and a CT scan of the mediastinum and abdomen.

Bone marrow trephine and aspirate was performed under full sterile conditions. The patient lay in the left lateral position and a Jamshidi needle was inserted under local anaesthetic to biopsy the marrow from the right anterior iliac crest. An

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*Author for correspondence.

†Present address: Department of Medicine, Gloucester Royal Hospital, Great Western Road, Gloucester.

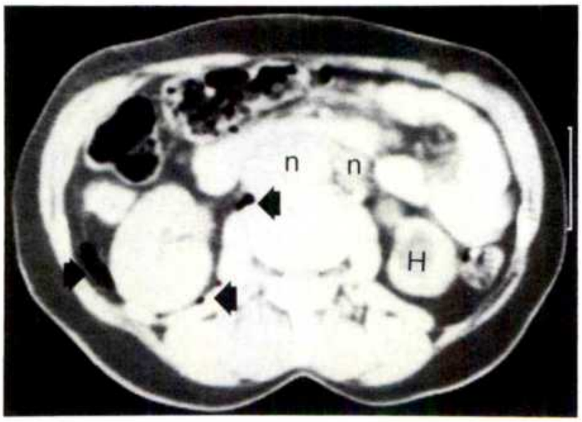

FIG. 1.

Computed tomography scan at the level of the right renal hilum shows posterior pararenal gas (arrows), enlarged para-aortic nodes (n) and left hydronephrosis (H) (L + 40, W 512).

adequate specimen of marrow was obtained with no immediate complications.

Twenty-four hours later the patient's mediastinum and abdomen were examined using a Siemens Somatom II CT scanner. The mediastinal appearances were normal. In the abdomen, in addition to showing para-aortic lymphadenopathy and an unexpected left hydronephrosis, the scan demonstrated locules of gas in the right posterior pararenal space extending on consecutive scans from the level of the right renal hilum inferiorly to the level of the iliac crest biopsy site (Figs 1 and 2).

The patient remained asymptomatic after the CT examination and has since commenced chemotherapy.

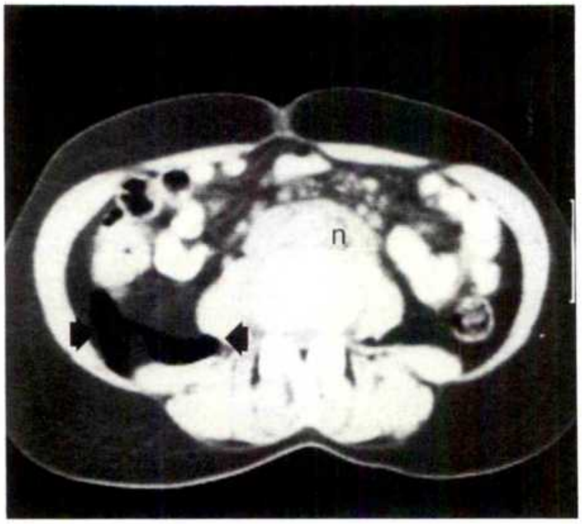

FIG. 2.

Scan 10 cm below that in Fig. 1 shows extensive gas in the posterior pararenal space (arrows) and further para-aortic nodes (n). At this level the perirenal space normally contains only fat (L + 40, W 512).

DISCUSSION

The retroperitoneum is divided by the anterior and posterior layers of the renal fascia into the anterior pararenal, perirenal and posterior pararenal spaces. The posterior pararenal space is bounded anteriorly by the posterior renal fascia, medially by the fusion of the transversalis fascia with the iliopsoas fascia and posteriorly by the transversalis fascia. The posterior pararenal space contains no organs and consists of only a thin layer of fat. The posterior pararenal space continues lateral to the lateroconal fascia as the properitoneal fat of the abdominal wall. Here it is visualised on plain abdominal radiographs as the "flank stripe".

Gas within the posterior pararenal space is, in itself, somewhat unusual. As the duodenum, ascending and descending colon and pancreas all lie within the anterior pararenal space, gas from these organs preferentially localises in this compartment (Meyers, 1974). Similarly, perirenal infection is, at least initially, confined by Gerota's fascia. Posterior pararenal space gas, when seen, is most commonly due to rectal perforation or to gas tracking down from the mediastinum and in such cases is usually bilateral. Unilateral left posterior pararenal space gas may be secondary to sigmoid colon perforation (Meyers, 1976).

In this case the gas was limited to the right posterior pararenal space and extended inferiorly to the level of the bone marrow biopsy site. Clinically, there was no evidence of bowel perforation and the patient's subsequent course was uneventful. Thus, it is most likely that the gas was air which had entered the posterior pararenal space as a result of direct penetration of the trephine through the iliac crest (Fig. 3). In addition to recording a further cause of pneumoretroperitoneum, this case demonstrates the

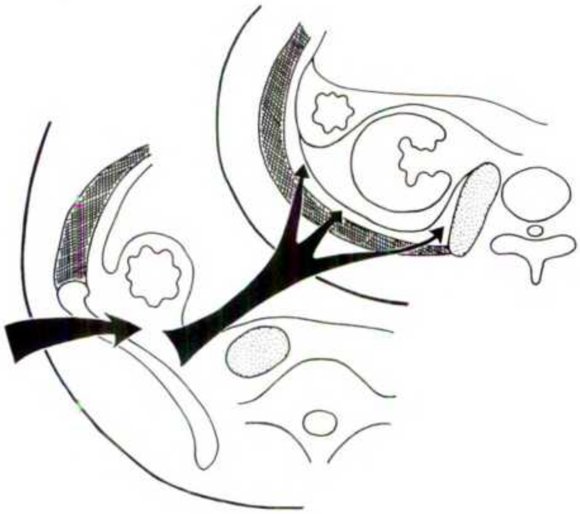

FIG. 3.

Diagram showing postulated route of retroperitoneal air.

ease with which any infection introduced by iliac crest biopsy could be widely disseminated and emphasises the necessity for scrupulous sterile technique.

ACKNOWLEDGMENTS

We would like to thank Dr T. K. Wheeler for permission to publish this case and Alison Emery for preparing the manuscript.

REFERENCES

LEZAK, M. B. & GOLDHAMMER, M., 1974. Retroperitoneal emphysema after colonoscopy. *Gastroenterology*, *66*, 118–120.

MEYERS, M. A., 1974. Radiological features of the spread and localisation of extraperitoneal gas and their relationship to its source. *Radiology*, *111*, 17–26.

——1976. *Dynamic Radiology of the Abdomen: Normal and Pathological Anatomy* (Springer-Verlag, New York), pp. 181–190.

PETERSON, N., ROHRMANN, C. A. & LENNARD, E. S., 1982. Diagnosis and treatment of retroperitoneal perforation complicating the double contrast barium enema examination. *Radiology*, *144*, 249–252.

POWNER, D. J., SNYDER, J. V., MORRIS, C. W. & GRENVIK, A., 1976. Retroperitoneal air dissection associated with mechanical ventilation. *Chest*, *69*, 739–742.

Percutaneous transhepatic cavography of dual obstruction of the inferior vena cava

By Tsutomu Araki, M.D., Kazushige Hayakawa, M.D., Sanshin Hayashi, M.D., Junichi Okada, M.D. and Guio Uchiyama, M.D.

Department of Radiology, University Hospital of Yamanashi

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Obstruction of the inferior vena cava (IVC) occurs in any segment, but more commonly in the infrarenal and diaphragmatic segments. However, occlusion in both segments has rarely been encountered. We have successfully opacified the intervening segment between two occluded segments, confirmed its patency and clarified its detailed anatomy by percutaneous transhepatic inferior vena cavography (PTIVC) in a patient.

CASE REPORT

A 52-year-old man presented with repeated episodes of thrombophlebitis in his lower extremities and prominent subcutaneous varices of the trunk. Laboratory data disclosed impaired hepatic and normal renal function: total serum bilirubin 2.9 mg/dl, direct bilirubin 1.6 mg/dl, alkaline phosphatase 465 IU/l, leucine aminopeptidase 125 IU/l, γ-glutamyl transpeptidase 293 IU/l, glutamate oxaloacetate transaminase 43 IU/l, glutamic pyruvic transaminase 26 IU/l, urea nitrogen 15 mg/dl and creatinine 0.5 mg/dl. Computed tomography of the upper abdomen revealed extensive calcification of the wall of the IVC, and occlusion at the diaphragm (Fig. 1). The hepatic, renal and supradiaphragmatic segments were well opacified following an intravenous infusion of contrast agent. The hemiazygous and abdominal subcutaneous veins were dilated. Ultrasonography also showed occlusion of the IVC and patency of its hepatic and renal segments (Fig. 2). The IVC was not identified by radionuclide angiography.

Inferior vena cavography was attempted via the femoral route. Because of multiple varices overlying the right inguinal area and the right side of the abdomen, the left femoral vein was catheterised. The catheter did not pass into the IVC. Left external iliac venography revealed an obstruction of the left common iliac vein, a large communicating vessel between both internal iliac veins, obstruction of the right common iliac vein and extensive collateral veins over the abdominal wall (Fig. 3). Consequently, computed tomography of the lower abdomen was carried out. Complete occlusion of both common iliac veins and the caudal end of the infrarenal IVC with extensive calcification was clearly shown. Although the patency of the hepatic and renal segments had been disclosed by computed tomography and ultrasonography, detailed anatomy of the IVC was required to assess the possibility of surgical correction and transluminal angioplasty.

Using a long 19-gauge needle with a Teflon sheath, percutaneous transhepatic puncture of the IVC was carried out under ultrasonic guidance in a similar fashion to percutaneous transhepatic portography. Contrast agent (30 ml) was injected through the sheath into the intervening patent segment of the IVC, which was clearly opacified together with both renal veins and tortuous retroperitoneal collateral veins (Fig. 4). The injection was repeated simultaneously with superior vena cavography via the jugular route, and biplane angiography was performed to reveal the occluded segment, measuring 10 mm long at the diaphragm. The venous pressure of the intervening patent segment was 350 mm H_2O. The sheath was withdrawn and gelatine sponge particles were injected into the needle track in the liver.

DISCUSSION

Although occlusion of the IVC is not rare, its dual obstruction in a patient has not been reported. Obstruction of the IVC may be due to the congenital

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Reprint requests to: Tsutomu Araki, Tamaho, Nakakoma, Yamanashi, Japan.

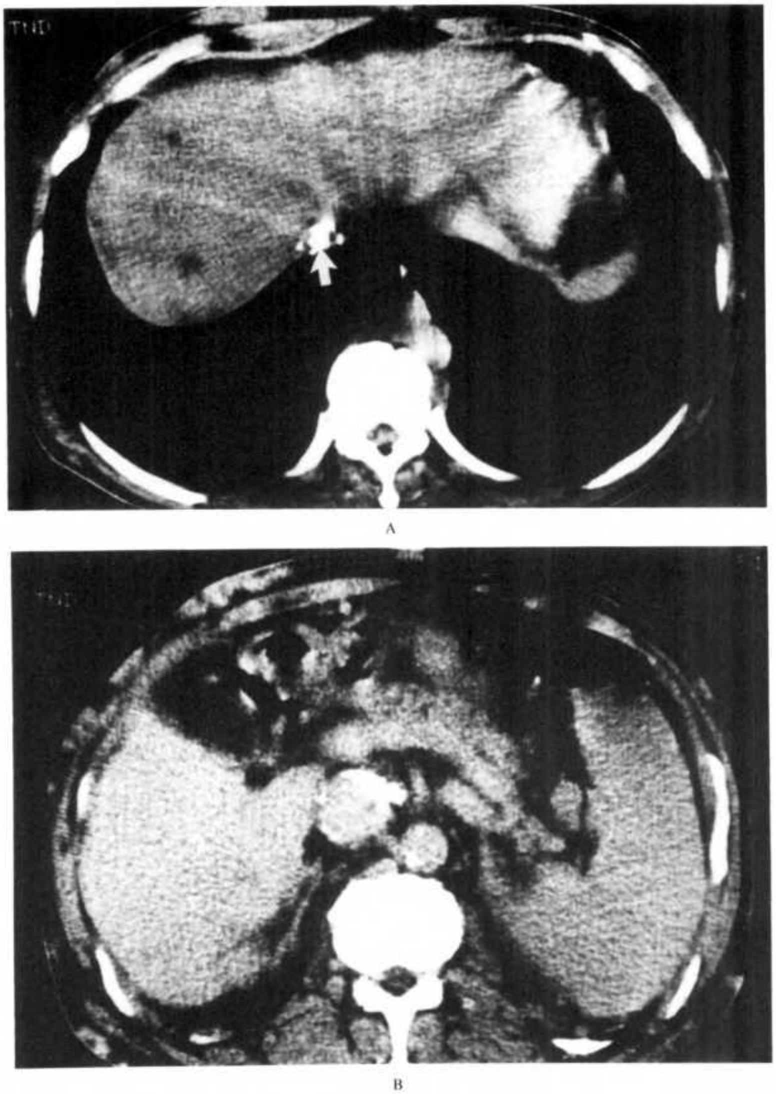

FIG. 1.

Computed tomogram of the upper abdomen. (A) Calcification of the diaphragmatic segment of the IVC is shown (arrow), but the lumen is absent. (B) Renal segment is patent despite extensively calcified wall.

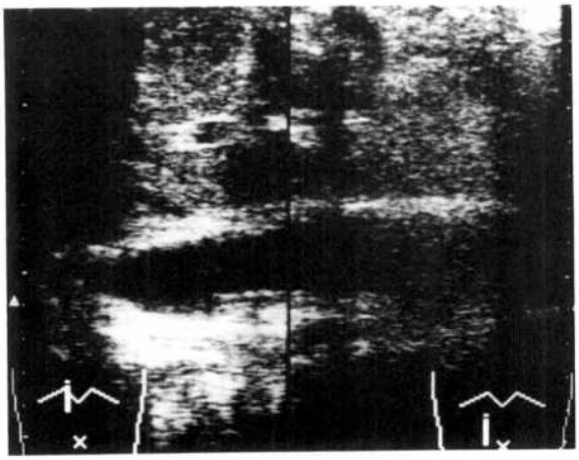

FIG. 2.

Sagittal cut of ultrasonography. Patency of the hepatic and renal segments of the IVC is confirmed. The IVC is narrowed towards the diaphragm.

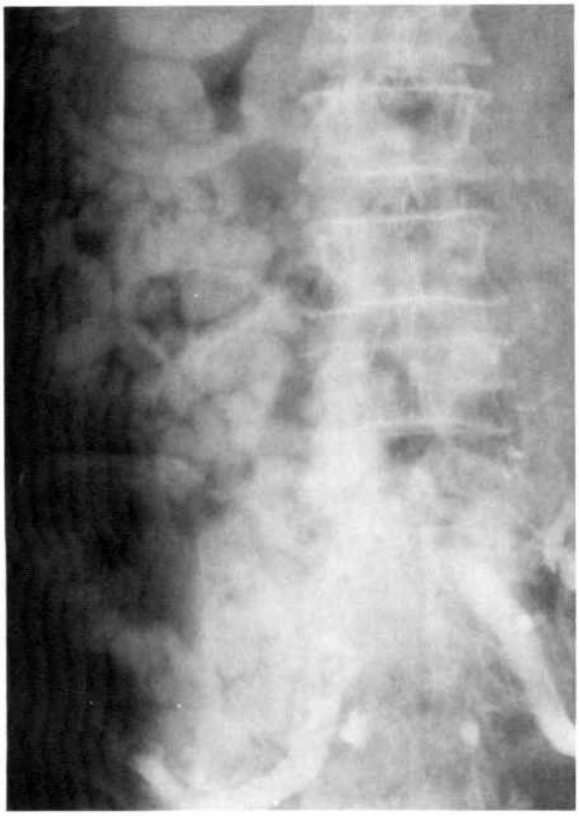

FIG. 3.
Late phase of left external iliac venography. Occlusion of both common iliac veins and extensive subcutaneous collateral veins are demonstrated.

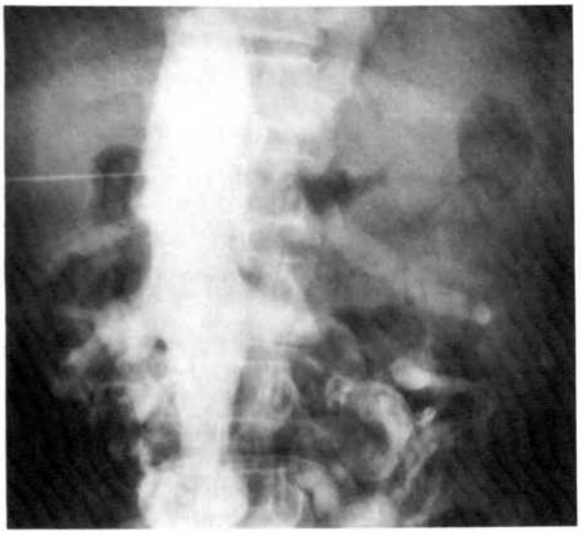

FIG. 4.
Renal and hepatic segments of IVC and retroperitoneal collaterals are opacified on PTIVC.

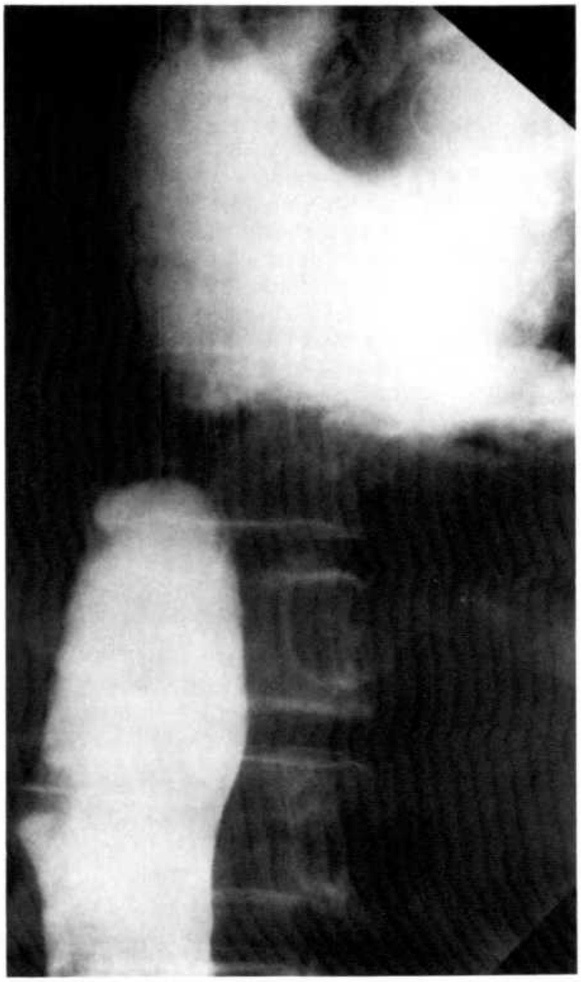

FIG. 5.
Simultaneous cavography disclosing that the occluded segment at the diaphragm is 10 mm thick.

absence of the hepatic segment (Anderson et al, 1961), congenital membrane (Hirooka & Kimura, 1970), thrombosis (Vujic et al, 1981), tumour thrombus (Madayag et al, 1979), or compression by an extrinsic mass. The calcification at the occluded diaphragmatic segment, repeated episodes of thrombophlebitis in the legs, a rather long occluded lower segment, and the coexisting occlusion of both common iliac veins (thrombophlebitis of which is a major source of pulmonary emboli (Mavor & Galloway, 1967)), suggest thrombosis complicating a congenital membrane as the most likely aetiology in this case.

Catheterisation of the vena cava is easily carried out from above via antecubital or jugular routes and from below via femoral or other ascending routes, when occlusion is suspected. Dual occlusion of the IVC, however, requires a different approach in order to

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clarify the detailed anatomy of the intervening patent segment and collateral veins. With experience from percutaneous transhepatic cholangiography and portography (Lunderquist & Vang, 1974), PTIVC can be safely carried out under ultrasonic guidance. Patency of the intervening segment is readily shown by computed tomography or ultrasonography. Its direct opacification, however, is necessary for detailed regional anatomy, and to show the length of occluded segments, the possible presence of a narrow communicating channel, and associated collateral vessels, and to select the treatment, which may be surgery (Iwahashi, 1981), transluminal angioplasty (Yamada et al, 1983), or medical care. Blood pressure in the intervening segment is also readily measured. Finally, this case stresses the necessity of a complete survey of the lower as well as upper abdomen by non-invasive imaging modalities before angiography, whenever obstruction of the diaphragmatic segment of the IVC is suspected since another occlusion may coexist.

REFERENCES

Anderson, R. C., Adams, P., Jr & Burke, B., 1961. Anomalous inferior vena cava with azygos continuation (infrahepatic interruption of the inferior vena cava). *Journal of Pediatrics, 59,* 370–383.

Hirooka, M. & Kimura, C., 1970. Membranous obstruction of the hepatic portion of the inferior vena cava. Surgical correction and etiological study. *Archives of Surgery, 100,* 656–663.

Iwahashi, K., 1981. Surgical correction of the inferior vena cava obstruction with Budd-Chiari syndrome. *Nippon Geka Hokan, 50,* 559–570.

Lunderquist, A. & Vang, J., 1974. Transhepatic catheterization and obliteration of the coronary vein in patients with portal hypertension and esophageal varices. *New England Journal of Medicine, 291,* 646–649.

Madayag, M. A., Ambos, M. A., Lefleur, R. S. & Bosniak, M. A., 1979. Involvement of the inferior vena cava in patients with renal cell carcinoma. *Radiology, 133,* 321–326.

Mavor, G. E. & Galloway, J. M. D., 1967. The iliofemoral venous segment as a source of pulmonary emboli. *Lancet, i,* 871–874.

Vujic, I., Stanley, J. & Tyminski, L. J., 1981. Computed tomography of suspected caval thrombosis secondary to proximal extension of phlebitis from the leg. *Radiology, 140,* 437–441.

Yamada, R., Sato, M., Kawabata, M., Nakatsuka, H., Nakamura, K. & Kobayashi, N., 1983. Segmental obstruction of the hepatic inferior vena cava treated by transluminal angioplasty. *Radiology, 149,* 91–96.

Renal embolisation for urinary fistula using alcohol (chemical nephrectomy)

By M. Rahman, F.R.C.S. (Ed.), D.M.R.D., F.R.C.R., S. R. Koneru, F.R.C.S. (Ed. & Glas.) and A. B. McEwan, F.R.C.S.

Departments of Diagnostic Radiology and Urology, Royal Infirmary, Blackburn, Lancashire BB2 3LR

(*Received November 1985*)

Therapeutic embolisation of renal arteries is well established in the management of renal cancer (Mazer et al, 1981). Various materials have been used and absolute alcohol, a relatively new agent, has been shown to be both effective and inexpensive (Ellman et al, 1981). It is technically simple to use, with little hazard to the patient. We report a case in which we performed renal embolisation using alcohol as an alternative to surgery in the management of ureteric fistula.

Case Report

A 59-year-old woman was diagnosed as having a carcinoma of the cervix in 1981 and she received a course of radiotherapy. Eighteen months later she was admitted to hospital with symptoms and signs of peritonitis. At laparotomy she was found to have perforation of the distal sigmoid colon resulting from radiation colitis. This was treated by transverse colostomy and peritoneal toilet. Three months later a sigmoid colectomy was performed followed by closure of the colostomy. Post-operatively, the patient developed severe frequency and urgency of micturition. Intravenous urography showed normally functioning kidneys except for slight dilatation of the left minor calyces, but her bladder was severely contracted and oedematous as a result of radiation cystitis, subsequently proved at cystoscopy. It was decided that urinary diversion offered the best chance of making the patient's life more comfortable.

At operation it was found impossible to mobilise the left ureter as it was embedded in dense fibrous tissue, again the result of irradiation. The small intestine was not suitable for the fashioning of an ileal conduit for the same reason. A right ureterostomy was, therefore, performed and the left ureter tied three times with linen thread just above the iliac vessels.

After a symptom-free interval of 1 week, the patient developed leakage of urine vaginally and was found to have a fistula between the left ureter and the vagina. The ureterostomy, however, functioned well and continued to do so. The post-operative period was further complicated by a deep-vein thrombosis which was treated with anticoagulants and compression bandages.

Correspondence to Dr M. Rahman, Department of Diagnostic Radiology

Having had four operations in 8 months, the last being followed by a deep-vein thrombosis, the patient did not appear to be suitable, either mentally or physically, to undergo further surgery. As there was satisfactory function of the right kidney it was decided to embolise the left kidney in an attempt to stop the leakage of urine per vaginam. This was successfully carried out under local anaesthesia by selective catheterisation of the left renal artery using a percutaneous femoral approach (Fig. 1). A post-embolisation angiogram showed stagnation of flow in the major arteries, truncation of segmental arteries and persistent parenchymal staining (Fig. 2).

The patient was free from her distressing symptom of urinary leakage within 24 h. She experienced loin pain for about 3 days after the procedure, followed by nausea, vomiting and a low-grade pyrexia. These were treated conservatively and she made a satisfactory recovery. During the following 18 months she remained free of urinary and cardiovascular complications.

DISCUSSION

Various materials have been used to achieve permanent occlusion of renal arteries: Gianturco steel coils (Mazer et al, 1981), bucrylate (Freeny et al, 1979), detachable balloons (White et al, 1979), autologous blood clot (Barth et al, 1977), absorbable gelatin sponge (Chuang et al, 1981) and gelfoam (Chuang & Wallace, 1981). Some of these agents are difficult to use while others have the potential danger of systemic embolisation with serious consequences. They have been employed mainly in the pre-operative management of the patients with renal carcinoma.

Alcohol embolisation, which has been used only in recent years, is effective and inexpensive. The procedure is technically simple and easy to perform. As far as we are aware, alcohol embolisation has not been carried out previously in the management of ureteric fistula.

We used 25 ml of absolute alcohol as embolising agent. This was injected in a fractionated dosage to minimise reflux. The volume of ethanol required for satisfactory embolisation was calculated from the body weight. A dose of 1 ml per 1.8 kg (4 lb) body weight is usually adequate (Ellman et al, 1981). We found it extremely useful to dissolve non-ionic contrast material in the ethanol prior to injection (Goldin et al, 1974) as fluoroscopic observation during the procedure is now considered mandatory (Ellman et al, 1981). As an indication that the amount and flow rate of ethanol was adequate, we observed (a) slowing of flow of ethanol in

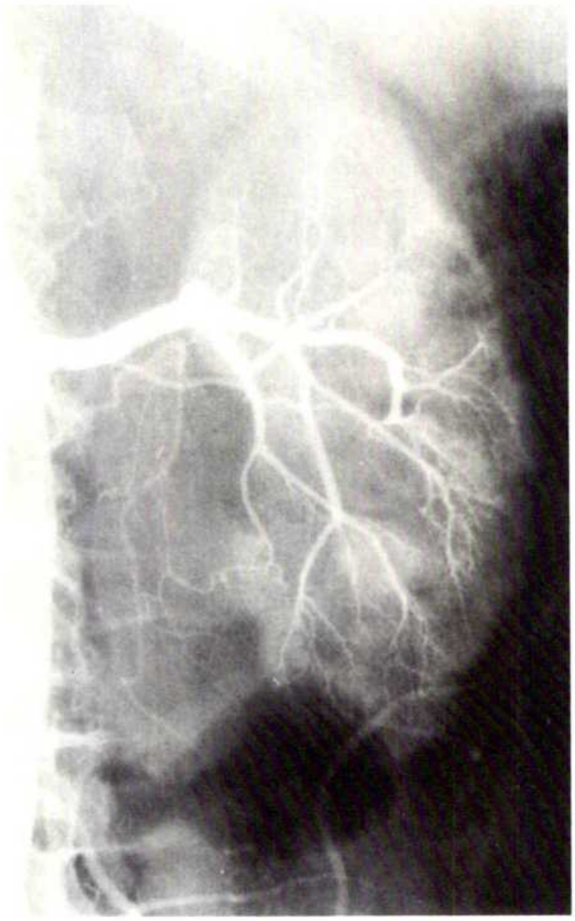

FIG. 1.

Preliminary angiogram showing normal renal artery and its branches.

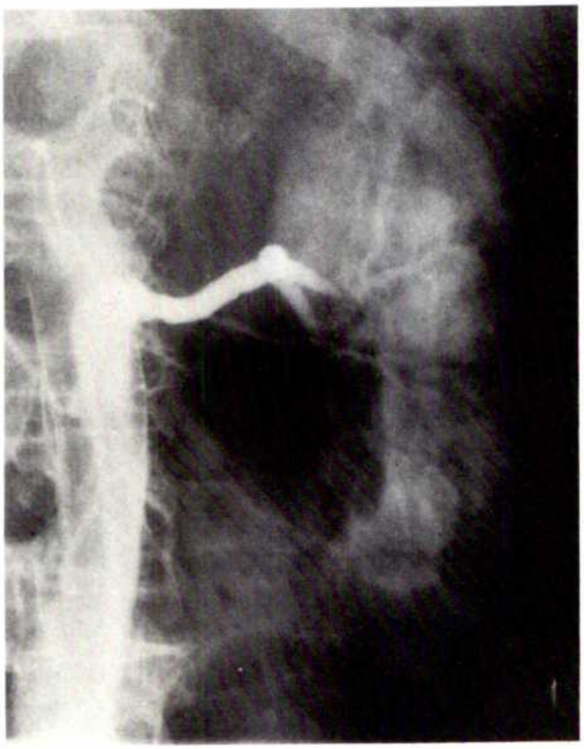

FIG. 2.

Post-embolisation angiogram: note truncation of segmental arteries, stagnation and parenchymal staining.

the renal artery and (b) development of reflux without any change in pressure or rate of injection. However, in the event of reflux of ethanol past the wedged catheter, the small amount entering the aorta or any other major artery should be rendered harmless by immediate dilution (Ellman et al, 1980)

Renal embolisation has been shown to be a suitable alternative to surgery for various non-malignant renal lesions, for example gross haematuria due to arterio-venous malformations, trauma or hypertension after renal transplantation (Lieberman et al, 1983; Fletcher et al, 1984). This is a further demonstration that such a procedure is useful in the management of the poor-risk patient with a urinary fistula.

Renal embolisation with alcohol may be carried out safely as an alternative method in the management of urinary fistula resulting from gynaecological and surgical procedures, especially if further surgical intervention is contraindicated. Assuming the availability of a radiologist experienced in catheterisation, the only prerequisite is a normally functioning contralateral kidney.

ACKNOWLEDGMENT

We wish to thank Miss L Aspinall for her invaluable help in preparing the manuscript

REFERENCES

BARTH, K H., STRANDBERG, J. D., WHITE, R. I., JR, 1977 Long term follow up of transcatheter embolisation with autologous clot. Oxycel and Gelfoam in domestic swine. *Investigative Radiology, 12,* 273–280

CHUANG, V P & WALLACE, S., 1981 Arterial infusion and occlusion in cancer patients. *Seminars in Roentgenology, 16,* 13–25.

CHUANG, V P., SOO, C. S. & WALLACE, S, 1981 Ivalon embolisation in abdominal neoplasms. *American Journal of Roentgenology, 136,* 729–733.

ELLMAN, B. A, GREEN, C. E., EIGENBRODT, E., GARRIOTT, J. C. & CURRY, T. A., 1980. Renal infarction with absolute alcohol. *Investigative Radiology, 15,* 318–322.

ELLMAN, B. A., PARKHILL, B. J, CURRY, T. S., MARCUS, P B. & PETERS, P. C, 1981. Ablation of renal tumours with absolute ethanol—a new technique. *Radiology, 141,* 619–626

FLETCHER, E. W L., THOMPSON, J F., CHALMERS, D. H. K, TAYLOR, H. M., WOOD, R. F. M. & MORRIS, P. J, 1984 Embolisation of host kidneys for the control of hypertension after renal transplantation. Radiological aspects. *British Journal of Radiology, 57,* 279–284.

FREENY, P C, BUSH, W. H., JR & KIDD, R., 1979. Transcatheter occlusive therapy of genitourinary abnormalities using isobutyl 2—cyanoacrylate (bucrylate). *American Journal of Roentgenology, 133,* 647–656.

GOLDIN, A. R., NAUDE, J. H. & THATCHER, G. N, 1974 Therapeutic percutaneous renal infarction. *British Journal of Urology, 46,* 133–135

LIEBERMAN, S. F., KELLER, F. S, PEARSE, H. D., FUCHS, E F., ROSH, J. & BARRY, J. M., 1983 Percutaneous vaso-occlusion for non-malignant renal lesions. *Journal of Urology, 129,* 805–809.

MAZER, M. J., BALTAXE, H A. & WOLF, G. L., 1981. Therapeutic embolisation of the renal artery with gianturco steel coils: limitations and technical pitfalls. *Radiology, 138,* 37–46.

WHITE, R. I., JR, KAUFMAN, S L, BARTH, K. H., DECAPRIO, V. & STRANDBERG, J. D., 1979. Embolotherapy with detachable silicone balloons *Radiology, 131,* 619–627.

1986, *The British Journal of Radiology*, 59, 943–944

SEPTEMBER 1986

Case of the month

A pain in the pelvis

By T. M. S. Geake, M.R.C.P., F.R.C.R.

Department of Radiology, Royal Adelaide Hospital, Australia

(*Received December 1985*)

A 36-year-old woman, whose only relevant past history was of a right tubal pregnancy, presented with a 6-month history of lower abdominal discomfort. Pelvic examination revealed a poorly defined mass in the right adnexal region, palpation of which induced paraesthesiae down the right leg.

Chest and abdominal radiographs were normal, as was an excretory urogram. Pelvic ultrasound was performed (Fig. 1) and followed by computed tomography (CT) after oral contrast medium and a single injection of 40 cm^3 Conray 420 (May & Baker Ltd) to outline the distal ureters and bladder base (Figs 2, 3).

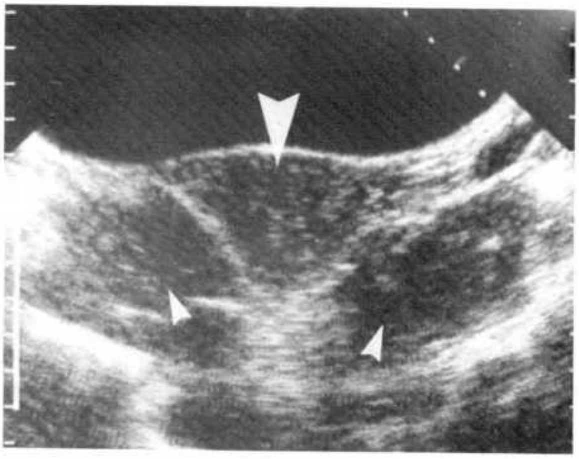

FIG. 1.

Transverse ultrasound scan above the pubic symphysis.

What abnormalities are shown and what is your diagnosis?

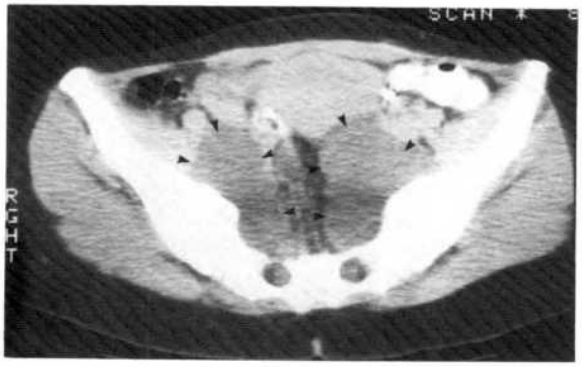

FIG. 2.

A CT scan at same level as Fig. 1.

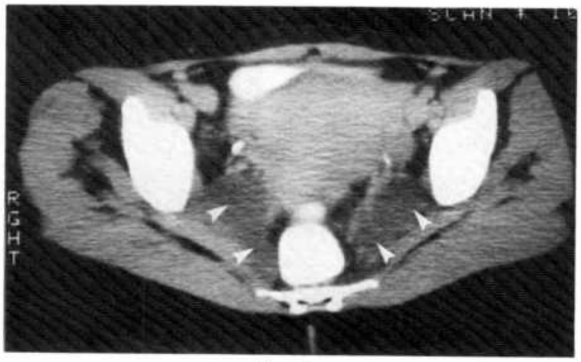

FIG. 3.

A CT section immediately above acetabulum.

Figure 1 shows two areas of reduced echogenicity lying behind and lateral to the bladder. A low-density mass is seen at these sites in Fig. 2, and the sacral foramina are large. Bilateral low-density masses are seen posteriorly in Fig. 3.

The appearances are those of plexiform neurofibromatosis, which is a form of generalised dysplasia of neuroectodermal and mesodermal tissue characterised by multiple nerve sheath tumours. Localised nervous tissue overgrowth may be fusiform and multiple in nature and form an intricate and communicating network, entrapping adjacent non-neural soft tissue. These lesions occur most commonly in the neck and limbs, and less often in the chest and abdomen (Kumar et al, 1983).

After making the diagnosis radiologically, a single café-au-lait spot was found on the patient's back, and a localised thickening of a peripheral nerve could be felt in the right buttock (Fig. 4).

DISCUSSION

Neurofibromatosis (von Recklinghausen's disease) has characteristic clinical manifestations and rarely presents a problem in diagnosis. Skin lesions may be absent in 10% of patients with a proven diagnosis of neurofibromatosis and 30% of patients have between one and six café-au-lait spots (Crowe & Schull, 1953). All, except one, previously reported cases of pelvic plexiform neurofibromatosis have exhibited generalised disease including skin stigmas. Our patient had a single skin lesion but on CT showed the characteristic features and distribution of pelvic plexiform neurofibromatosis as previously described (Paling, 1984; Lanzieri & Hilal, 1984).

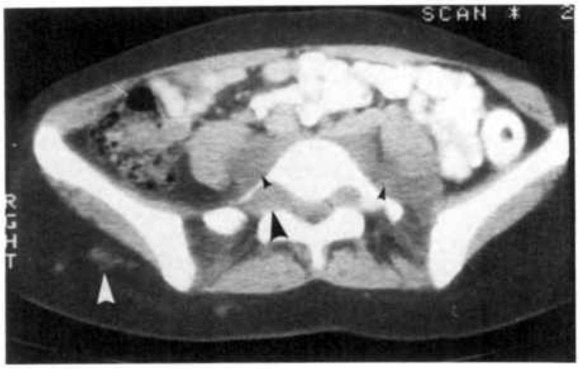

FIG. 4.

A CT scan at a level above Fig. 2 shows displacement of the psoas muscles by lower-density soft tissue (small arrowheads), enlarged sacral foramina (large black arrowheads) and an enlarged soft-tissue density in the fat posterior to the right ilium (white arrowhead).

The presence of pelvic side-wall masses of high echogenicity in the absence of acoustic shadowing on ultrasound should suggest a fat-containing tumour.

Simple and plexiform neurofibromas on CT have attenuation values of 20–30 HU and may enhance following contrast by 10 HU. When such lesions are homogeneous and have the distribution and configuration typical of neurofibromatosis, histological confirmation is unnecessary since it may be hazardous (Paling, 1984). Low-attenuation areas may result from haemorrhage or necrosis developing in areas of sarcomatous degeneration within the mass (17–30 HU) (Coleman et al, 1983), a high content of lipid-rich Schwann cells within the tumour (5–17 HU) or fat incorporation within the tumour (−50–0 HU) (Kumar et al, 1983). In general, the higher the fat content of a mass (*i.e.* the lower the attenuation value), the less likely the mass is to be malignant.

In this patient, since large areas of the mass exhibited attenuation values of −20–0 HU with no evidence of associated bone destruction, it was considered to be benign and biopsy confirmation was not sought.

REFERENCES

COLEMAN, B. G., ARGER, P. H., DALINKA, M. K., OBRINGER, A. C., RANEY, B. R. & MEADOWS, A. T., 1983. CT of sarcomatous degeneration in neurofibromatosis. *American Journal of Roentgenology*, *140*, 383–387.

CROWE, F. W. & SCHULL, W. J., 1953. Diagnostic importance of café-au-lait spots in neurofibromatosis. *Archives of Internal Medicine*, *91*, 758–766.

KUMAR, A. J., KUHAJDA, F. P. MARTINEZ, C. R., FISHMAN, E. K., JEZIC, D. V. & SIEGELMAN, S. S., 1983. Computed tomography of extracranial nerve sheath tumours with pathological correlation. *Journal of Computer Assisted Tomography*, *7*, 857–865.

LANZIERI, C. F. & HILAL, S. K., 1984. Computed tomography of the sacral plexus and sciatic nerve in the greater sciatic foramen. *American Journal of Roentgenology*, *143*, 165–168.

PALING, M. R., 1984. Plexiform neurofibroma of the pelvis in neurofibromatosis: CT findings. *Journal of Computer Assisted Tomography*, *8*, 476–478.

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Memoranda from the British Committee on Radiation Units and Measurements

Effective quality factor for neutrons

(*Received April 1986*)

The British Committee on Radiation Units and Measurements (BCRU) has taken note of the statement from the recent meeting of the International Commission on Radiological Protection in Paris (ICRP, 1985), which recommended that the effective quality factor, $\bar{Q}$, for neutrons should be increased by a factor of two as compared with the values given in ICRP Publication 21 (ICRP, 1973). Having considered this statement, BCRU recommends that no change should be made to the quality factor for neutrons in radiation protection practice in the UK for the time being, that the quality factors should continue to be based on information in ICRP Publication 21, and that the quality factors used should be recorded from now on.

There are two aspects to this recent ICRP recommendation about which BCRU feels some concern.

(1) The ICRP has stated its intention to undertake a further review of biological and other information: "The implications of this information will be considered as part of a larger review of recommendations to be undertaken by the Commission over the next four years or so" (ICRP, 1985). It is considered, therefore, that it would be premature to change this one figure when other recommendations may appear in the next few years.

(2) The biological action of neutrons is associated with the recoil nuclei and other charged particles released. It is not clear why the quality factor for neutrons should be changed while the quality factor for other particles, such as protons, deuterons, alpha particles etc., are not changed.

There are also matters relating to the biological data and their interpretation that are outside the remit of BCRU, but which influenced its decision. In earlier publications ICRP have stated the following.

> "The values of Q and $\bar{Q}$ have been selected on the basis of relevant values of relative biological effectiveness but they also take account of the fact that dose-equivalent limits are based on extrapolations from *higher* absorbed doses at which the deleterious effects *in man* can be directly assessed. The values of Q are therefore *not* necessarily representative of relative biological effectiveness for other observed effects, such as stochastic effects *in animals* at *low* levels of absorbed dose" (ICRP, 1977).

Nevertheless, in association with their recommendation for changing the quality factor for neutrons, the ICRP referred to certain information in the statement from their 1985 Paris meeting:

> "The information now available on the relative biological effectiveness (RBE) for neutrons for a variety of *cellular effects in vitro*, and for life shortening *in the mouse*, is being reviewed by the Commission" (ICRP, 1985).

Prima facie, there appears to be some inconsistency, since this statement appears to imply a change in the philosophy as regards the determination of quality factors.

When preparing this memorandum, BCRU looked for guidance towards those organisations that have a direct concern with the biological effects of radiation and their interpretation.

(1) A group of experts appointed under Article 31 of the Euratom Treaty has the responsibility for advising the Commission of the European Communities (CEC) on basic safety standards relating to radiation protection. It is understood that this group is not at present preparing any new recommendations which would lead to a modification of the Council Directive laying down the safety standards for the health protection of the general public and workers against the dangers of ionising radiation (CEC, 1981).

(2) The National Radiological Protection Board (NRPB) has advised that any change in Q for neutrons should be delayed until the final ICRP decision is known (NRPB, 1986).

(3) The Medical Research Council's Committee on Effects of Ionising Radiation (CEIR) Radiation Biology Subcommittee has this subject on its agenda but has not yet made any comment or recommendation.

There is an obligation now for all member states of the European Community to comply with Council directives. These cover many different fields, and one of them is radiological protection, for which the directive at present in force is the Council Directive of July 15, 1980 (CEC, 1981). In the context of this memorandum, this Directive contains exactly the same numerical data as ICRP Publication 21 (ICRP, 1973), on which it was based. At the moment it appears that other countries in the European Community are not going to take any action to change quality factors for neutrons. So, bearing in mind its concern regarding the recent ICRP (1985) recommendation and the lack of any evidence that emergency action is called for to change neutron quality factors, BCRU recommends that no change should be made to quality factors in the UK until the current Council Directive (CEC, 1981) is amended.

At some time in the future a more consistent and accurate set of quality factors may become available. When this happens, BCRU will recommend and plan the implementation of the consequent changes in the UK, in collaboration with its European partners. In preparation for that time, BCRU recommends that, as soon as possible, dosimetry laboratories should make careful records of the quality factors that they have used in the past and those that are in current use. Also that in statements of dose equivalent and its derived quantities in such things as personal dose records and published papers, the quality factors used should also be stated. Only in this way will it be possible to combine past and future dose records and achieve long-term consistency in radiation protection dosimetry.

Although CEC (1981), based as it is on ICRP Publication 21 (1973), contains data from which quality factors for different energies and types of radiations can be derived, all that many

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Address for reprints and correspondence: J. E. Burns, Secretary, BCRU, National Physical Laboratory, Teddington, Middlesex TW11 0LW.

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workers need to know is that for photons and electrons $\bar{Q}$ is equal to unity, while for neutrons of unknown energy, $\bar{Q}$ is equal to 10. In some circumstances it may therefore be easy to quote the actual values of the quality factors used, but in other situations it may be simpler to state that they were derived from data in the Council Directive of 1980 on radiological protection (CEC, 1981) Whatever type of statement is made, it must be unambiguous.

BCRU will keep this question of quality factors under review, and will issue further memoranda when necessary.

Membership of BCRU during the preparation of this memorandum was. T. E. Burlin (Chairman), R. J. Berry (Vice-Chairman), J. E. Burns (Secretary), D. M. Ackery, G E. Adams, J. A. Dennis, S. C. Ellis, K E. Halnan, J. R. Harvey, A. McNair, D H. Pearson, D. E Watt and T. O. Young.

REFERENCES

CEC, 1981 Council Directive of July 15, 1980, 80/836/Euratom (Official Journal of the European Communities L 246 of 17.9.1980). *Radiological Protection—21* (Commission of the European Communities, Luxembourg).

ICRP, 1973. *Data for Protection Against Ionizing Radiation from External Sources. Supplement to ICRP Publication 15.* ICRP Publication 21 (Pergamon Press, Oxford).

——1977. *Recommendations of the International Commission on Radiological Protection.* ICRP Publication 26 (Pergamon Press, Oxford).

——1985. Statement from the 1985 Paris meeting of the ICRP *British Journal of Radiology*, 58, 910.

NRPB, 1986. *New Radiation Quantities Recommended by ICRU for Practical Use in Radiological Protection· Their Implementation in the United Kingdom.* Guidance Standard NRPB GS5 (National Radiological Protection Board, Chilton).

New quantities in radiation protection and conversion coefficients

(*Received April 1986*)

In its Report 39 published in February 1985, the International Commission on Radiation Units and Measurements (ICRU) put forward four new quantities for use in radiation protection from external sources (ICRU, 1985). The British Committee on Radiation Units and Measurements (BCRU) recommends that these quantities should be adopted for use in the UK, together with the conversion coefficients given in this memorandum

DEFINITIONS

For environmental and area monitoring, two quantities were defined by the ICRU

The ambient dose equivalent, $H^*(d)$, at a point in a radiation field, is the dose equivalent that would be produced by the corresponding aligned and expanded field, in the ICRU sphere at a depth, *d*, on the radius opposing the direction of the aligned field. The meanings of the terms expanded and aligned fields are discussed later in this memorandum. The quantity is suitable for measuring strongly penetrating radiation, using an instrument with an isotropic response A depth of 10 mm is recommended for $H^*(d)$, which may be written as $H^*(10)$

The directional dose equivalent, $H'(d)$, at a point in a radiation field, is the dose equivalent that would be produced by the corresponding expanded field in the ICRU sphere at a depth, *d*, on a radius in a specified direction. This quantity is suitable for measuring weakly penetrating radiation The instrument used will typically have a detector situated beneath a thin layer of plastic, and its response will not be isotropic. A depth of 0.07 mm is recommended for $H'(d)$, which may be written as $H'(0\ 07)$.

For individual or personal monitoring, the ICRU defined two further quantities.

The individual dose equivalent, penetrating, $H_p(d)$, is the dose equivalent in soft tissue below a specified point on the body at a depth, *d*, that is appropriate for strongly penetrating radiation. A depth of 10 mm is recommended for $H_p(d)$, which may be written as $H_p(10)$.

The individual dose equivalent, superficial, $H_s(d)$, is the dose equivalent in soft tissue below a specified point on the body at a depth, *d*, that is appropriate for weakly penetrating radiation A depth of 0.07 mm is recommended for $H_s(d)$, which may be written as $H_s(0.07)$

In the above definitions, the ICRU sphere is a 30 cm-diameter, tissue-equivalent sphere with a density of 1 g/cm^3 and a mass composition of 76.2% oxygen, 11.1% carbon, 10.1% hydrogen and 2.6% nitrogen (ICRU, 1980).

In ICRU Report 39 (ICRU, 1985), strongly and weakly penetrating radiations are distinguished by the relation between skin dose equivalent and effective dose equivalent received by a body with a given orientation irradiated in a uniform and unidirectional field. Radiation is *strongly penetrating* if the dose equivalent received by a small area of the sensitive layer of the skin is *less* than 10 times larger than the effective dose equivalent. Conversely, radiation is *weakly penetrating* if the dose equivalent received by a small area of the sensitive layer of the skin is *more* than 10 times larger than the effective dose equivalent

CONCEPTS OF EXPANDED AND ALIGNED FIELDS

In order to avoid many of the difficulties that had arisen from the definitions of some earlier quantities proposed for use in radiation protection, two new concepts have been incorporated into the definitions of ambient and directional dose equivalent.

The first concept is that of an *expanded* field This relates to the fact that the sensitive volume of a radiation dosemeter is often so small that it may be regarded as making a measurement at a single point in a radiation field. In radiation protection, the measured value at this point is then used to infer what effect the radiation would have on a large body, such as a man, at the location of the measurement. The expanded-field concept simplifies this situation by assuming that the field over the whole irradiated body has the same fluence and energy distribution as the field at the point of measurement. In the definition of both ambient and directional dose equivalents, the irradiated body is a 30 cm-diameter tissue-equivalent sphere: a standard phantom intended to simulate a human trunk.

The second new concept is that of an *aligned* field. Many instruments intended to be used for the measurement of strongly penetrating radiation are designed to have an isotropic response, *i.e.* to respond equally to radiation from all directions. This directional dependence will clearly be different from that of a dose equivalent quantity in a large body. For example, the response at a point 1 cm deep in a large body will be highest for those components of a radiation field that are incident through the nearest surface. In the definition of ambient dose equivalent, the concept of an aligned field is introduced; this has the same fluence and energy distribution as the actual field, but differs from it in that all the radiation is assumed to be from a single direction. The concept therefore has the effect of making this quantity correlate with a measurement using an instrument with an isotropic response. Another important and intentional consequence of the aligned field concept is that the ambient dose equivalent, $H^*(10)$, is unlikely to be less than the dose equivalent received from the actual radiation field at a point 10 mm beneath the surface of an irradiated body.

CONVERSION COEFFICIENTS (FACTORS)

In view of the likelihood that it may be some time before any further information is published by ICRU on this matter, BCRU believes that it would be helpful to users in the UK at this time to provide conversion coefficients to enable calibrations in terms of the new quantities to be derived from those in quantities currently disseminated by national standardising laboratories.

It would be unfortunate if national bodies adopted different approaches and different numerical data. The BCRU therefore welcomed the seminar on radiation protection quantities for external exposure sponsored by the Commission of the European Communities, the proceedings of which have been published in *Radiation Protection Dosimetry*, Vol. 12, No. 2, 1985. One outcome of this seminar was formulae for deriving conversion coefficients for ambient and directional dose equivalent. Values derived using these formulae are given in the appendix to this memorandum. Should ICRU make recommendations on conversion coefficients (factors) in the future, BCRU will review the situation and issue a further memorandum.

CALIBRATION PROCEDURES

When an instrument which is always used free-in-air, such as an environmental monitor, is calibrated in $H^*(10)$ or $H'(0.07)$ in a known radiation field and by application of the conversion coefficients given in the appendix, it should be calibrated free-in-air; the scatter from an ICRU sphere is already included in the conversion coefficients. In contrast, when personal dosemeters, which are always worn on the surface of the body, are calibrated in $H_p(10)$ or $H_s(0.07)$, the calibration should be performed on an appropriate phantom, or, alternatively, allowance should be made for the backscatter from the phantom.

For the calibration of personal trunk dosemeters on the surface of an appropriate phantom irradiated by a broad unidirectional beam normal to the surface, $H_p(10)$ may be taken as equal to $H^*(10)$. For the calibration of personal dosemeters on the surface of an appropriate phantom irradiated by a broad unidirectional beam of weakly penetrating radiation, $H_s(0.07)$ may be taken as equal to $H'(0.07)$.

RELATION TO DOSE-LIMITING QUANTITIES

In environmental and area monitoring, the value of $H^*(10)$ at a point would not underestimate, nor seriously overestimate, the effective dose equivalent that would be received by a person at that location. The value of $H'(0.07)$ would give an estimate of the dose equivalent to uncovered skin.

In individual or personal monitoring, the maximum value of $H_p(10)$ on the trunk may overestimate the effective dose equivalent to that individual, but it will not underestimate it; if it is possible to identify the region of the body surface at which this maximum value occurs, a personal dosemeter should be worn there. A measurement of $H_s(0.07)$ would give an estimate of the dose equivalent to skin exposed to the same radiation field.

RECOMMENDATIONS

The BCRU recommends that the four new quantities defined in ICRU Report 39 should be adopted in radiation protection practice. In implementing this recommendation, in order that radiation protection dosimetry should be consistent throughout the UK, it also recommends that the conversion coefficients given in the appendix to this memorandum should be used when recalibrating existing instruments and when reporting or recording the results of measurements; they should also be used by manufacturers when designing new instruments. These recommendations do not preclude the use of other quantities in certain circumstances, such as fluence or air kerma for calibrating secondary standard or reference dosemeters.

This memorandum supersedes the previous BCRU memorandum on the subject (BCRU, 1982), which recommended an interim procedure to be adopted until the ICRU published details of the new quantities.

More detailed information about the conditions of use of the conversion coefficients, and about such matters as the calibration of instruments and dosemeters for measuring the new ICRU quantities, should become available later from other organisations (*e.g.* NRPB, 1986).

Membership of BCRU during the preparation of this memorandum was: T. E. Burlin (Chairman), R. J. Berry (Vice-Chairman), J. E. Burns (Secretary), D. M. Ackery, G. E. Adams, J. A. Dennis, S. C. Ellis, K. E. Halnan, J. R. Harvey, A. McNair, D. H. Peirson, D. E. Watt and T. O. Young.

APPENDIX: CONVERSION COEFFICIENTS

The conversion coefficients in this appendix enable calibrations in terms of the new quantities to be derived from those in quantities currently disseminated by primary standardising laboratories. The recommended conversion coefficients for monoenergetic photons, neutrons and electrons result from a careful survey of all the calculated data available at the end of 1985. Data are also provided for beta radiation. For monoenergetic photons and neutrons, empirical mathematical functions have been fitted to available calculated data, weighted where appropriate. These functions are provided for the convenience of users, and they have no physical or biological basis; their derivation is discussed by Wagner et al (1985). Tabulated values and graphs are derived from the formulae.

Photon radiation

For monoenergetic photons with energies between 10 keV and 10 MeV, the relationship between ambient dose equivalent at 10 mm depth, $H^*(10)$, and air kerma free-in-air, K_a, is given by:

$$\frac{H^*(10)}{K_a} = \frac{x}{ax^2+bx+c} + d.\arctan(gx) \quad \text{Sv/Gy} \qquad (1)$$

where $a = 1.465$, $b = -4.414$, $c = 4.789$, $d = 0.7006$, $g = 0.6519$, arctan is in radians, and $x = \ln(E/E_0)$, where E = photon energy (keV) and $E_0 = 9.85$ keV. This relationship is illustrated in Fig. 1, and some values are given in Table I.

For unidirectional monoenergetic photons with energies between 10 keV and 250 keV, the relationship between directional dose equivalent at 0.07 mm depth in the ICRU sphere on the radius opposing the direction of the incident radiation, $H'(0.07)$, and air kerma free-in-air, K_a, is given by:

$$\frac{H'(0.07)}{K_a} = a + bx + cx^d.\exp(gx^2) \quad \text{Sv/Gy} \qquad (2)$$

where $a = 0.9505$, $b = 0.09432$, $c = 0.2302$, $d = 5.082$, $g = -0.6997$, and $x = \ln(E/E_0)$, where E = photon energy (keV) and $E_0 = 9.85$ keV. This relationship is illustrated in Fig. 2, and some values are given in Table I. It should be noted that the conversion coefficients given by Equation 2 apply only for the simple irradiation geometry often used for calibrations, *i.e.* unidirectional radiation with the reference point on the radius of the ICRU sphere opposing the direction of the incident field; values for other irradiation geometries are being derived and will become available later from other organisations.

Neutron radiation

For monoenergetic neutrons with energies between 0.025 eV and 20 MeV, the relationship between ambient dose equivalent

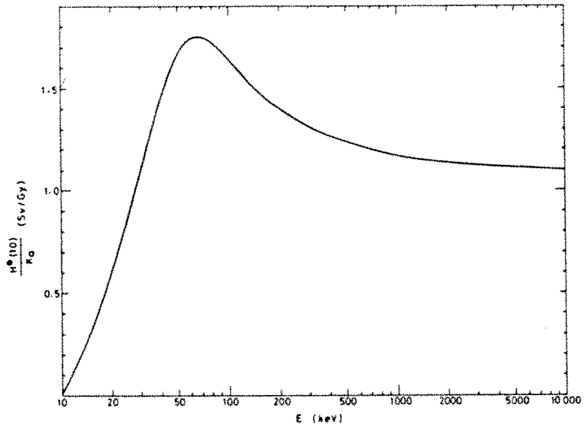


FIG. 1.

Conversion coefficient $H^*(10)/K_a$ for monoenergetic photon radiation calculated from Equation 1 and plotted against photon energy E.

TABLE I

CONVERSION OF AIR KERMA TO AMBIENT AND DIRECTIONAL DOSE EQUIVALENT FOR PHOTONS OF ENERGY E, CALCULATED FROM EQUATIONS 1 AND 2

E (keV)	$H^*(10)/K_a$ (Sv/Gy)	$H'(0.07)/K_a$ (Sv/Gy)
10	0.01	0.95
15	0.32	0.99
20	0.60	1.05
25	0.86	1.13
30	1.10	1.22
40	1.47	1.41
50	1.67	1.53
60	1.74	1.59
70	1.75	1.61
80	1.72	1.61
90	1.68	1.58
100	1.65	1.55
125	1.56	1.48
150	1.49	1.42
200	1.40	1.34
250	1.35	1.32
300	1.31	—
500	1.23	—
662	1.20	—
1000	1.17	—
1250	1.16	—
3000	1.13	—
5000	1.11	—
10000	1.10	—

Note: the values in Column 3 apply only for unidirectional photons and with the reference point on the radius of the ICRU sphere opposing the direction of the incident field.

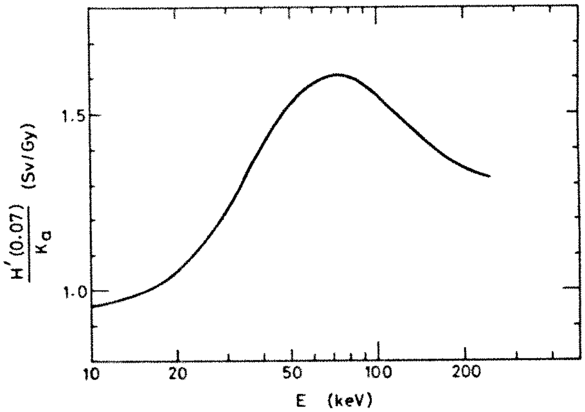


FIG. 2.

Conversion coefficient $H'(0.07)/K_a$ for monoenergetic photon radiation calculated from Equation 2 and plotted against photon energy E; these values apply only for unidirectional photons and with the reference point on the radius of the ICRU sphere opposing the direction of the incident field.

at 10 mm depth, $H^*(10)$, and neutron fluence free-in-air, ϕ, is given by:

$$\log_{10}[H^*(10)/\phi] = \frac{a}{1+(b+cx)^2} + \frac{d}{1+\exp(f-gx)} + \frac{h}{1+\exp(j-kx)} \qquad (3)$$

where $H^*(10)/\phi$ is in pSv cm^2, and $a = 1.02$, $b = 0.0102$, $c = 0.208$, $d = 2.33$, $f = 9.56$, $g = 1.98$, $h = 0.187$, $j = 93.3$, $k = 13.1$, and $x = \log_{10}(E)$, where E = neutron energy (eV). This relationship is illustrated in Fig. 3, and some values are given in Table II.

No coefficients are given for the conversion of neutron fluence to directional dose equivalent, $H'(0.07)$, since the skin dose is unlikely to be limiting for broad-beam irradiation by neutrons. The reason for this is that at no neutron energy is the ratio of the dose-equivalent at 0.07 mm depth likely to be 10 times that at 10 mm, and current dose limits are such that this ratio must exceed 10 before skin dose is limiting.

Beta radiation

Table III gives coefficients for beta radiation from a small plane source, to convert absorbed dose to air, D_a, measured free-in-air, into directional dose equivalent at 0.07 mm depth in the ICRU sphere on the radius opposing the direction of incident radiation, $H'(0.07)$. The variation of this coefficient with maximum beta-ray energy is illustrated in Fig. 4.

The values given here agree with those recommended for use with the three secondary standard beta-ray sources available from the National Physical Laboratory (Rossiter, 1986), and are based on recommendations put forward in three previous BCRU memoranda on protection-level beta-ray dosimetry (BCRU, 1974, 1977a,b). The basic recommendations still apply, that the primary standard should be an ionisation chamber measuring absorbed dose to air, free-in-air, but that recommended conversion coefficients should be used so that beta-ray dosemeters can be calibrated in terms of dose equivalent at the time of their calibration against secondary standard beta-ray sources. However, in order to bring them

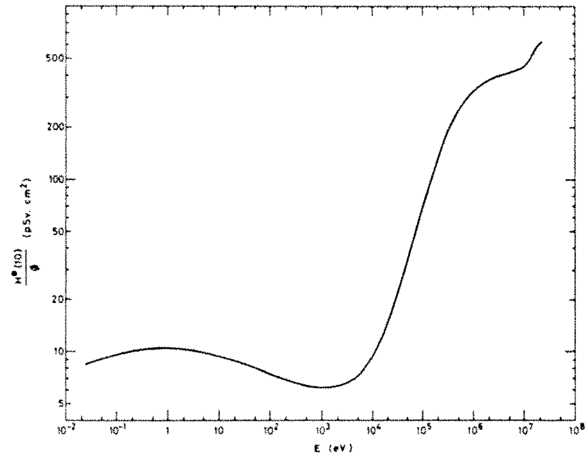


FIG. 3.

Conversion coefficient $H^*(10)/\phi$ for monoenergetic neutron radiation calculated from Equation 3 and plotted against neutron energy E.

TABLE II

CONVERSION OF FLUENCE TO AMBIENT DOSE EQUIVALENT FOR NEUTRONS OF ENERGY E, CALCULATED FROM EQUATION 3

E	$H^*(10)/\phi$ (pSv cm^2)
0.025 eV	8.4
0.1	9.6
1.0	10.5
10	9.4
100	7.4
500	6.3
1.0 keV	6.1
2.0	6.2
5.0	7.2
10	9.4
20	14.7
24	17.0
50	34.1
100 keV	70.2
144	100
200	135
250	161
500	250
565	265
1.0 MeV	328
1.2	345
2.0	382
2.5	393
2.8	398
5.0	415
10.0 MeV	451
14.8	553
19	609
20	615

TABLE III

CONVERSION OF ABSORBED DOSE TO AIR INTO DIRECTIONAL DOSE EQUIVALENT FOR BETA RADIATION

Maximum beta-ray energy (MeV)	$H'(0.07)/D_a$ (Sv/Gy)
0.1	0.10
0.15 (^{147}Pm)	0.22
0.2	0.40
0.3	0.72
0.4	1.00
0.5	1.16
0.57 (^{204}Tl)	1.22
0.6	1.23
0.7	1.24
0.8	1.25
0.9	1.25
1.0	1.25
1.5	1.25
2.0 (^{90}Sr + ^{90}Y)	1.25

Note: the conversion coefficients apply only for beta radiation from a small plane source and with the reference point on the radius of the ICRU sphere opposing the direction of the incident field.

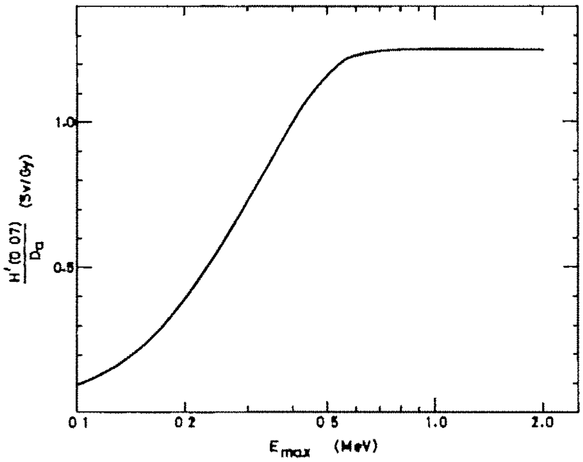


FIG. 4

Conversion coefficient H' (0.07)/D_a for beta radiation plotted against maximum beta-ray energy E_{max}; these values apply only for beta radiation from a small plane source and with the reference point on the radius of the ICRU sphere opposing the direction of the incident field.

into line with the new ICRU quantities, the depth at which the dose equivalent is calculated has been changed from an average between 5 mg/cm^2 and 10 mg/cm^2 to a depth of 7 mg/cm^2 (0.07 mm) beneath the surface. Some restrictions on the application of these coefficients are discussed in BCRU (1977a).

High-energy electron radiation

It is unlikely that there will be many occasions when it is necessary to measure the dose-rate in a high-energy electron beam for protection purposes. Moreover, no calibrations are available for protection-level dosemeters for these conditions. Data from Harder (1970) and Peixoto et al (1981) indicate that there is very little variation in the ratio of $H^*(10)$ to electron fluence with the energy of high-energy electrons. If it is required, it may be helpful in establishing a conversion coefficient to note that a single value, 330 pSv cm^2, may be used to convert electron fluence to ambient dose equivalent at 10 mm depth, $H^*(10)$, for electron radiation at all energies between 5 MeV and 50 MeV.

REFERENCES

BCRU, 1974. Conversion of beta-ray dose rates measured in air to dose rates in skin. *Physics in Medicine and Biology, 19,* 748–752

—1977a Further discussion on the conversion of beta-ray dose rates measured in air to dose rates in skin. *Physics in Medicine and Biology, 22,* 101–103.

—1977b. Quantities for the calibration of protection-level beta-ray dosemeters. *Physics in Medicine and Biology, 22,* 544–546

—1982. SI units for radiation protection—an interim measure. *British Journal of Radiology, 55,* 376–377

HARDER, D., 1970. Some general results from the transport theory of electron absorption. Proceedings of the Symposium on Microdosimetry, 1969, Stresa. Ed by H G Ebert (Council of the European Communities, Brussels), pp. 567–594.

ICRU, 1980. *Radiation Quantities and Units.* ICRU Report 33 (International Commission on Radiation Units and Measurements, Washington).

——1985. *Determination of Dose Equivalents Resulting From External Radiation Sources.* ICRU Report 39 (International Commission on Radiation Units and Measurements, Washington).

NRPB, 1986. New radiation quantities recommended by ICRU for practical use in radiological protection: their implementation in the United Kingdom. Guidance Standard NRPB GS5 (National Radiological Protection Board, Chilton).

PEIXOTO, J. E., BLOHM, R, ABOU MANDOUR, M. & HARDER, D., 1981 Dose equivalent index for fast electrons. *Health Physics, 40,* 27–39.

ROSSITER, M J, 1986. Private communication (National Physical Laboratory, Teddington).

WAGNER, S. R, GROSSWENDT, B., HARVEY, J R, MILL, A J, SELBACH, H.-J & SIEBERT, B. R L., 1985. Unified conversion functions for the new ICRU operational radiation protection quantities *Radiation Protection Dosimetry, 12,* 231–235.

1986, *The British Journal of Radiology*, 59, 951–955 SEPTEMBER 1986

Short communication

Single photon emission computed tomographic imaging and volume estimation of the thyroid using fan-beam geometry

By S. Webb, M. A. Flower, R. J. Ott, M. D. Broderick, A. P. Long, B. Sutton and *V. R. McCready

Joint Department of Physics and *Department of Nuclear Medicine, Institute of Cancer Research and Royal Marsden Hospital, Downs Road, Sutton, Surrey

(*Received March 1986*)

The diagnosis of thyroid disease is usually determined from planar gamma-camera images of the distribution of ^{99}Tc^m pertechnetate using a pinhole or parallel-hole collimator. The high magnification possible for a small organ imaged with a pinhole collimator means that high spatial resolution is obtainable However, the three-dimensional spatial distribution of cold or hot regions within the thyroid is difficult to determine. Pinhole camera images give only a qualitative indication of the functioning volume of thyroid tissue, a parameter vital for the accurate dosimetry of radioiodine therapy. Clinical examination can give only a poor estimate of anatomical volume which may relate only indirectly to the volume containing radioactivity. Hamburger and Hamburger (1985) have noted that dosimetry is often largely empirical due to the difficulty of estimating the mass of thyroid tissue irradiated. The limitations of planar scintigraphy can be overcome by performing tomographic imaging. It has already been shown (Ott et al, 1986b) that positron emission tomography of the distribution of ^{124}I within the thyroid can achieve a spatial resolution of the order of 1 cm throughout the section and yield an estimation of thyroid volume with ~ 5% accuracy for uniform distribution of tracer and ~ 12% accuracy for multinodular disease. The limiting factor affecting dosimetry was shown by this study to be estimation of the biological half-life rather than the error in estimating the volume of functioning tissue. Positron tomography may well, in time, replace gamma-camera SPECT because of increased resolution with depth, especially with the development of multiwire proportional camera systems and generator-produced positron emitters (Ott et al, 1986a). In the meantime, however, gamma-camera SPECT is the widely available tomographic modality for imaging the functional distribution of radionuclides.

In this paper we demonstrate that SPECT can yield clear information on the three-dimensional distribution of thyroid disease and give an estimation of thyroid volume. The technique used to determine functional volume is explained together with an estimate of the accuracy of the measurement.

MATERIALS AND METHODS

Data acquisition

A special purpose collimator has been designed to perform SPECT in fan-beam geometry with the explicit aim of improving spatial resolution without sacrificing sensitivity. The collimator has holes which converge in the plane of rotation of the camera but which are parallel in the orthogonal direction. The focal length of the converging holes is 60.6 cm measured from the front surface of the collimator. The physical performance of this collimator has already been reported (Broderick, 1984; Webb et al, 1985a). In summary, using a radius of rotation of 25 cm the resolution was ~ 15 mm full width half maximum with little variation across the field of view. The volume sensitivity was some 30% greater than for a corresponding low-energy general purpose parallel-hole collimator. The limited field of view makes this approach valuable for small-part imaging.

For data acquisition the collimator was attached to a GE 400A gamma camera interfaced to a GE STAR computer system A 20% pulse height analyser window was centred on the ^{99}Tc^m photopeak. Sixty-four views were acquired in 180° rotation with the arc of rotation extending from patient right to patient left symmetrically about the anterior view. This limited-angle SPECT acquisition scheme was used in preference to a full 360° rotation because the thyroid is close to the anterior wall of the neck. A similar rationale for using 180° acquisition arises in cardiac imaging (Tamaki et al, 1982). Our experience in liver SPECT where semicircular arcs of full 360° acquisition data were reconstructed (Ott et al, 1983) has shown this to improve image contrast. The data were stored in 64 × 64 matrices with a pixel size of either 6.4 mm or 3.2 mm, the latter being used if data were captured using a times-two zoom facility. The use of the latter was dependent on the apparent extent of the thyroid seen in pinhole imaging. Typically, between 100 MBq and 200 MBq of ^{99}Tc^m were administered per patient and 64 projections of 15 s duration were collected The uptake in the thyroid ranged from 2% to 6%. Five patients were imaged and the technique was verified by imaging phantoms (spheres of diameters 1, 2, 3, 4 and 5 cm and three-dimensional thyroid phantoms) containing known volumes of activity.

Data reconstruction and display

Before reconstruction, each dataset was corrected for camera non-uniformity and drift of the electronic centre of rotation. For reconstruction and analysis, data were transfered from the STAR computer to a VAX 750 computer for which special purpose reconstruction software was written. Reconstruction was performed by a method of convolution and back-projection in which the shape of the frequency window could be adjusted (Webb, 1982) In particular, the cut-off frequency, F_w, could be controlled independently of the shape of the roll-off of a Hamming frequency-window ($W(F)$)

$$W(F) = \alpha + (1-\alpha)\cos(\pi F/F_w)$$

where $F_w = \gamma \cdot F_n$, and F_n is related to the reciprocal of the projection sampling interval. Detailed dependences on these parameters have been published by Broderick (1984). For the reconstructions in this paper we set $\gamma = 1$ and $\alpha = 0.54$, and it was arranged that data up to the Nyquist frequency were optimally used by a suitable choice of F_c. From each corrected dataset 64 transaxial slices were generated. In practice, 32 slices were reconstructed centred about the mid-line of the camera and these were then "stretched" to produce 64 slices with each slice repeated sequentially. The reason for this unusual scheme is to enable the reconstructed pixel size to be half the projection (detector) pixel size without incurring the penalty of a geometric distortion in the axial direction. Software was also constructed to generate coronal and sagittal datasets and, additionally, to interpolate 64×64 images to 256×256 for display.

For some purposes it was useful to visualise the external surface of the thyroid as a three-dimensional solid. Software to implement this has been constructed based on the package MOVIE. BYU from Brigham Young University. The software allows for the production of shaded-surface or wire-frame images. Three-dimensional images can be viewed from any orientation and dynamically rotated.

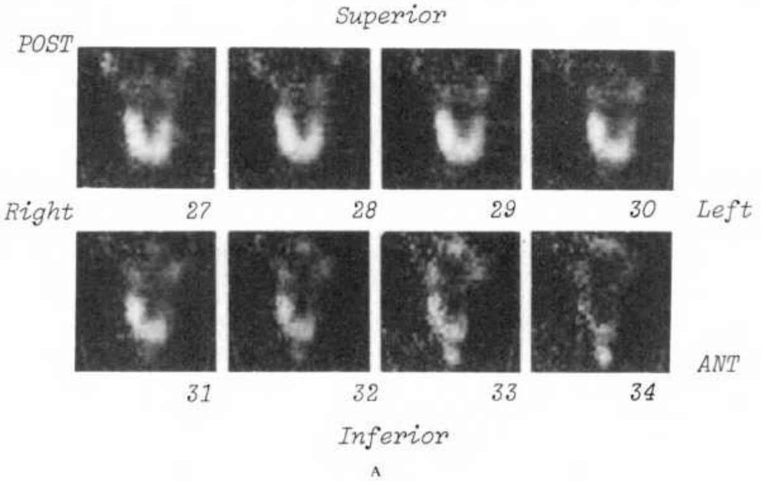
Determination of thyroid volume

The determination of functioning volume is hampered by several physical difficulties which lead to the classic problem of determining the edge of a distribution in the presence of background, noise and finite spatial resolution. The simplest volume measurement arises from summing the volume of all volume elements (voxels) with reconstructed count value greater than some pre-set value, expressed as a percentage (T) of the maximum reconstructed value. The volume (V) so determined is clearly a function of T, but experience from positron tomography has led to the observation that the true volume occurs at a break in slope of the V versus T curve or correspondingly a change in the value of $\mathrm{d}V/\mathrm{d}T$ (Webb et al, 1985c). The same technique was applied to SPECT imaging. It was not appropriate to use the "two step" technique described by Lowry (1983) and Webb et al (1985b) as applied to estimating liver volume because of the relatively small size of the thyroid.

RESULTS

Image data

Typically it was found that the tomographic images yielded more precise depth information on the spatial location of disease. The spatial resolution within each tomographic plane was, however, inferior to that in planar pinhole imaging. In general, the coronal slices were most useful since the thyroid can easily be identified by its location relative to the uptake in the salivary glands and a sternal-notch marker. Summing the



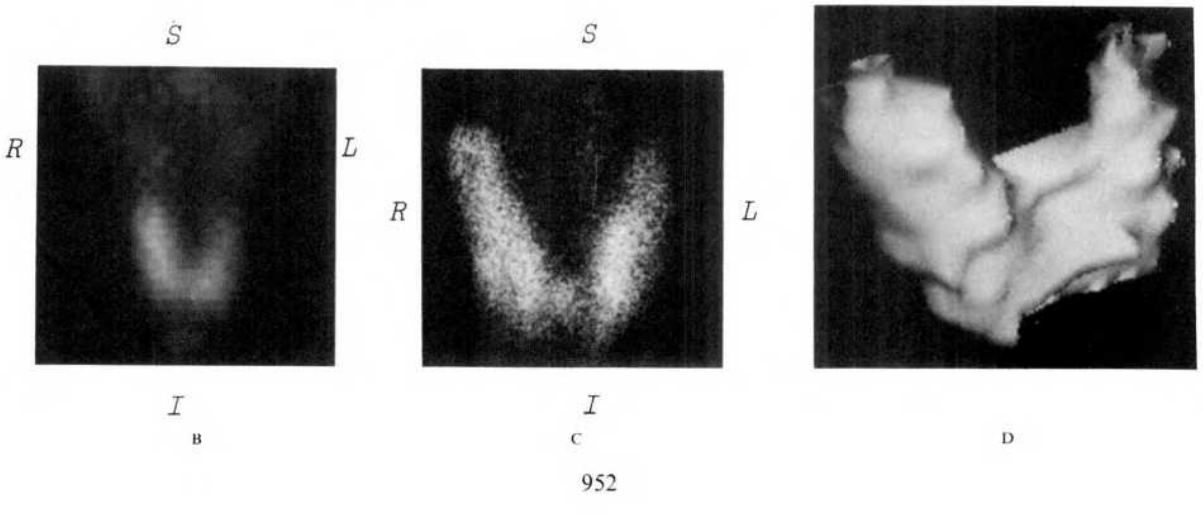


FIG. 1. *Case 1.*

(A) Eight coronal slices, numbers 27–34, (B) summed coronal slices (over frames 20–44), (C) pinhole planar image, (D) 3D shaded contour image. The slice numbers increase as the coronal images move from the most posterior to the most anterior slice.

information in contiguous coronal slices yielded an image similar to the pinhole image. In some cases it was possible to isolate a particular cold region to a small number of coronal slices. By making reference to the sternal-notch marker the precise depth of a region of interest could be determined.

As a typical case study Fig. 1 illustrates these findings. In Fig. 1A are shown coronal slices 27 to 34 of Case 1. It can be seen that the right lobe is larger and lying further anteriorly than the left and that there is a cold region in the upper left lobe. The marker shows in slices 33 and 34. Figure 1B shows the sum of the coronal data indicating much reduced contrast compared with the coronal slices. (These summed coronal data are the AP view which would be obtained if the photons were unattenuated.) Figure 1C presents the planar pinhole image for comparison. Figure 1D is a shaded-surface three-dimensional display of the whole reconstructed thyroid and is one "still" frame from the dynamic movie. This disease was confirmed by ultrasound imaging to be a multinodular goitre.

Figure 2 illustrates Case 2, displaying a left lobe which is much hotter than the right. The right lobe only appears in five coronal slices (29 to 33) whereas the left lobe appears in 10 (26 to 35). Since the slice thickness is 3.2 mm, approximate dimensions of the lobes are established. While the relative uptake of the two lobes can be found from the pinhole image (Fig. 2B) or the summed coronal image (Fig. 2C) (if it were assumed that the lobes were at the same depth), only from the tomographic data can one assess the precise location of the defect. The disease was a toxic left lobe.

Volume measurements

It was found for all patients that the plot of volume versus threshold exhibited a break of slope at threshold T_1. Furthermore, the value of T_1 varied only marginally between 42.8% and 45.2%. If the distribution in the thyroid were imagined to be a uniform spherical uptake of activity then one would expect (Webb et al, 1985c) that

$$-V^{-2/3}\mathrm{d}V/\mathrm{d}T = \text{constant}.$$

Despite the obvious non-spherical shape of the thyroid, this was found to hold approximately for each of the five patients studied and for a range of threshold between 32% and 58%. The value of the constant was between 0.1 and 0.3. The behaviour of V and $\mathrm{d}V/\mathrm{d}T$ versus T for Case 1 is shown in Fig. 3. This technique was used to estimate the volume of the thyroid and the data are shown in Table I. The disease type is also indicated in Table I (CUS indicating ultrasound confirmation). The use of the "break-in-slope" method was confirmed by visually inspecting all the tomographic data when the appropriate threshold, T_1, was used. The value of $(\mathrm{d}V/\mathrm{d}T)_{T_1}$ at the threshold T_1 can be used to estimate the percentage error in the measurement of functioning volume and these data are also shown in Table I. Clearly, as the estimated volume increases, the error on its measurement also increases.

The values of $(\mathrm{d}V/V)_{T_1}$ are shown in Table I for an error in threshold of 1%. The percentage error in volume is approximately linear with threshold close to T_1. Hence, taking

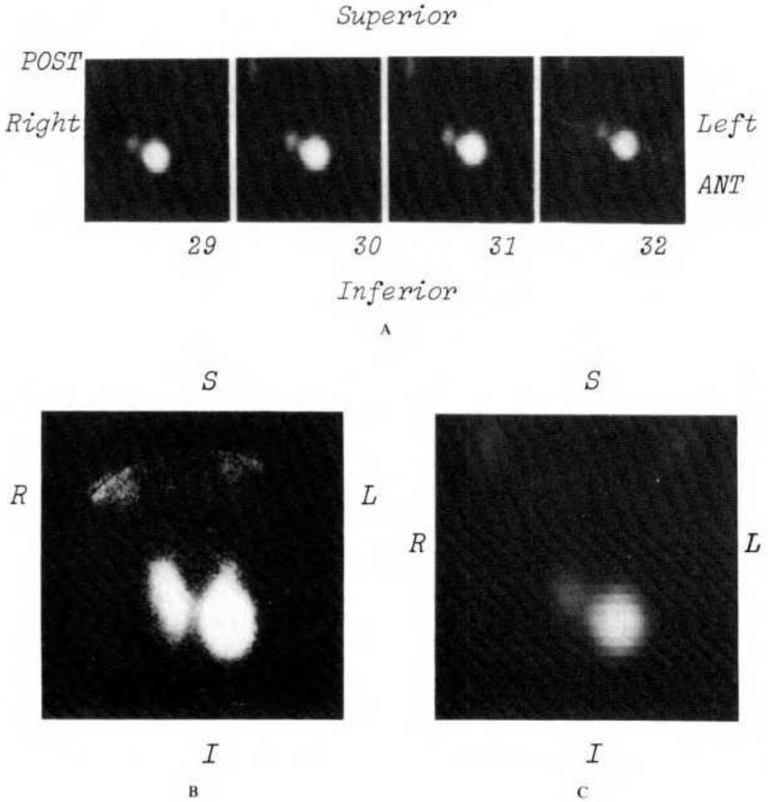


FIG. 2. *Case 2.*

(A) Four coronal slices, numbers 29–32, (B) pinhole planar image, (C) summed coronal slices (over frames 20–44). The slice numbers increase as the coronal images move from the most posterior to the most anterior slice.

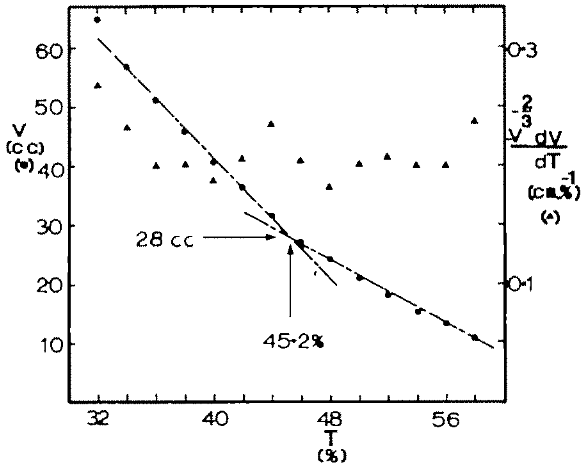


FIG. 3. *Case 1*
Plot of V versus T and $-V^{-2/3}\,dV/dT$ versus T.

a mean value of $(dV/V)_{T_1}$ together with the range of values of the threshold T_1, the maximum error in volume estimation is ~ 14% for thyroids with volumes between 15 ml and 30 ml

DISCUSSION AND CONCLUSIONS

It has been shown that SPECT can usefully generate information on the distribution of uptake in the thyroid gland which cannot be obtained by planar scintigraphy More importantly perhaps, the tomographic data form the basis for estimating the functioning volume of the thyroid with approximately 15% accuracy In order to compute the dose to the thyroid in radioiodine therapy, all that is required in addition to the thyroid volume is a measure of percentage thyroid uptake and biological half-life. The uptake is measurable to within 10% and a biological half-life of 6 days is conventionally used (Pireda et al, 1979). It is likely that the error in this assumption, however, is now the limiting factor affecting thyroid dosimetry. Before the development of tomographic imaging methods (SPECT or PET), the functioning volume was the principal unknown. Additionally there may be a difference in the functional volume given from analysing SPECT data using $^{99}Tc^m$ and the functional volume for iodine dosimetry This is a further reason for establishing the measurement of volume using iodine-labelled positron-emitting pharmaceuticals High-energy SPECT is a possible compromise, but again there are associated difficulties.

TABLE I

DATA PERTAINING TO THE MEASUREMENT OF FUNCTIONING VOLUME

Case	T_1 (%)	V_{T_1} (ml)	$-(dV/dT)_{T_1}$ (ml/%)	$(dV/V)_{T_1}$ (%)	Disease
1	45.2	28.0	1.85	6.82	multinodular goitre (CUS)
2	42 8	16.5	0.72	4.23	toxic left lobe
3	44.4	16.5	0.78	4.56	multinodular goitre
4	43 2	19 5	1.31	6 39	multinodular goitre (CUS)
5	44 2	22.5	1.58	6 57	multiloculated cystic lesion

CUS, confirmed on ultrasound image.

We should like to add two riders to the proposed method for estimating functioning volume Firstly, from our experimental data using spheres of known volume, the value of T_1 giving the true volume has been found to vary between 39% and 43% for spheres whose diameters are larger than the resolution of the SPECT data, but to increase to 50% for smaller spheres. The warning is clear for clinical work where the spatial extent of parts of a thyroid and/or its multinodular nature might lead to unresolved components of the images. The variation in T_1 almost certainly arises from this cause. Additionally, the break in slope is sometimes difficult to observe but, in the absence of any clearer criterion, is the preferred technique for estimation of functioning volume.

So far we have considered the use of the measured functional volume for estimation of whole thyroid radiation dose assuming a uniform uptake of the radionuclide in the functioning tissue. Our images show that in many cases the distribution is non-uniform and hence such estimation would give an average radiation dose to the thyroid. By using local regions of interest it is possible to delineate local regions whose uptake is increased or decreased and to calculate intrathyroid radiation doses using the volume and uptake values for such a region It should be emphasised, however, that using quantitative intrathyroid data is a non-trivial extension which needs to consider the image degradation from photon attenuation and scatter together with any other features which lead to a loss of quantitation

REFERENCES

BRODERICK, M D., 1984. An evaluation of a converging/parallel collimator attached to a rotating gamma camera, for high resolution single photon emission computed tomography. M Sc Thesis, University of London.

HAMBURGER, J. I & HAMBURGER, S. W, 1985. Diagnosis and management of large toxic multinodular goiters. *Journal of Nuclear Medicine*, *26*, 888–892.

LOWRY, C. A., 1983. The determination of organ volume, radioactive content and concentration using emission tomography M.Sc. Thesis, University of Surrey.

OTT, R. J., BATEMAN, J. E., BATTY, V., CLACK, R, FLOWER, M. A., LEACH, M. O., MARSDEN, P. K, MCCREADY, V. R., WEBB, S., SHARMA, H. & SMITH, A., 1986a. 3D positron emission tomography—preliminary results *British Journal of Radiology*, *59*, 419–422.

OTT, R. J., FLOWER, M A., KHAN, O., KALIRAI, T., WEBB, S, LEACH, M. O & MCCREADY, V R., 1983. A comparison between 180 and 360 data reconstruction in single photon emission computed tomography of the liver and spleen. *British Journal of Radiology*, *56*, 931–937.

OTT, R. J., BATTY, V., WEBB, S., FLOWER, M. A., LEACH, M. O., CLACK, R., MARSDEN, P K, MCCREADY, V R., BATEMAN, J. E., SHARMA, H & SMITH, A., 1986b. Measurement of radiation dose to the thyroid using positron emission tomography *British Journal of Radiology*, in press.

PIREDA, G, CLAVRIA, H J, ROCHA, A. F. & HERBERT, J. C., 1979. *Textbook of Nuclear Medicine Clinical Applications* (Lea and Febiger, Philadelphia), pp. 30–35.

TAMAKI, N., MUKAI, T, ISHII, Y., FUJITA, T., YAMAMOTO, K, MINATO, K., YONEKURA, Y., TAMAKI, S., KAMBARA, H., KAWAI, C. & TORIZUKA, K., 1982 Comparative study of thallium emission myocardial tomography with 180 and 360 data collection. *Journal of Nuclear Medicine, 23,* 661–666.

WEBB, S., 1982. A modified convolution reconstruction technique for divergent beams. *Physics in Medicine and Biology, 27,* 419–423

WEBB, S., BRODERICK, M. D. & FLOWER, M. A., 1985a. High resolution SPECT using divergent geometry *British Journal of Radiology, 58,* 331–334.

WEBB, S., FLOWER, M. A., OTT, R. J., LEACH, M. O., FIELDING, S., INAMDAR, R., LOWRY, C. A. & BRODERICK, M D, 1985b. A review of studies in the physics of imaging by single photon emission computed tomography. *Proceedings of the Symposium Recent Developments in Medical and Physiological Imaging, April 1985,* Ed. by M. R. Goff & R. P. Clark (Taylor and Francis Ltd, London).

WEBB, S., OTT, R. J, FLOWER, M. A., LEACH, M. O, MARSDEN, P. K. & MCCREADY, V. R., 1985c. Verification of a technique for the measurement of functioning thyroid volume using positron emission tomography. *Medical and Biological Engineering and Computing, 23,* Suppl. 2, 1397–1398

Book reviews

Handbook of Radiologic Orthopaedic Terminology. By R. F. Kilcoyne and E. Farrar, pp 144+index, 1986 (Year Book Medical Publishers Inc., Chicago), £16.50.
ISBN 0–8151–5030–X

The price of £16.50 may seem a lot to pay for this economically produced, slim softback, especially as it consists simply of line drawings and a "typewriter" style of text. However, the contents are worth every penny, providing a list of orthopaedic terms illustrated by line drawings. Where relevant, there are brief descriptions of the mechanism of injuries and the importance or otherwise of complete reduction of fractures or dislocations. Thus, when reporting metacarpal fractures, the authors explain why 40° of angulation is acceptable in fractures of the fifth metacarpal, whereas fractures of the second and third require complete reduction.

The amount of space devoted to a region depends entirely on the number of descriptive and eponymous terms associated with it. Thus, the upper limb needs 50 pages whereas the spine receives only five. However, those five pages save us hunting through a major work to remind us of such terms as a Chance fracture. Particularly valuable is a clear description of the principal pelvic fractures, a frequent pitfall for the unwary.

In addition to trauma there are, for example, drawings of the arches and angles of the foot, helping us to distinguish our pronated feet from our rocker-bottoms. After reading this book we can talk with renewed authority about self-tapping screws, gamekeeper's thumbs, not to mention that up-market lesion, the chauffeur's fracture.

The authors aimed at producing a "quick reference *vade mecum*", and in this they have succeeded admirably. Every trainee should have access to it when he starts reporting fractures and with it he will be able to beat those inveterate name-droppers, the orthopaedic surgeons, at their own game, without getting a swan-neck deformity, or a midnight fracture.

J. T. PATTON

Pocket Atlas of Rheumatology. By Dieter Wessinghage, pp. vii+230, 1985 (Georg Thieme Verlag, Stuttgart), DM 30.
ISBN 3–13–671601–9

This is a compact book of unusual type. It is aimed at non-rheumatologists and is a pictorial guide to the features that may be found in the joints and tendons in various forms of arthritis. There is a brief commentary accompanying the illustrations However, it is for the quality of the pictorial work that this book is notable. The illustrations, by the author, are superb, demonstrating the clinical, surgical and pathological features very well This is probably the best illustrated book I have seen on rheumatology. Radiologists will find the radiographs clear but unexciting

There is an interesting section on historical landmarks in the early description of these diseases and a series of tables illustrates the continental system of staging their progression. In summary, it is a book for a quick browse to remind one of the various features of arthritis, tendonitis and bursitis, but not of the systemic aspects of rheumatology.

P J. L. HOLT

1986, *The British Journal of Radiology*, *59*, 957–958 SEPTEMBER 1986

Correspondence

(The Editors do not hold themselves responsible for opinions expressed by correspondents)

Metastatic carcinoma from unknown primary site

THE EDITOR—SIR,
Snee and Vyramuthu (1985) report the clinical course and impact of treatment of patients presenting with metastatic carcinoma from an unknown primary site. In the treatment of bone pain by local radiotherapy they suggest from a retrospective review of the case notes that fractionated radiotherapy is superior to single-dose treatment, with a response of 90% compared with only 25%, respectively.

A prospective randomised trial has recently been completed at the Royal Marsden Hospital comparing a multiple-fraction regime of 30 Gy in 10 daily fractions with a single fraction of 8 Gy for the relief of metastatic bone pain (Price et al, 1986). In 288 randomised patients with bone pain, evaluated using a self-assessment questionnaire, no significant difference was found in incidence, duration or quality of pain relief.

The difference in results between the data from Edinburgh and our own may reflect in part the problems associated with the assessment of pain by retrospective case history review. It is also important to consider criteria for selection for single-fraction treatment, which, outside a randomised study, is often reserved for elderly or moribund patients. In addition, the numbers of patients receiving either single- or multiple-fraction treatment and more detail of the doses used would be of value before attributing difference in response to the different dose prescriptions alone.

Clearly the use of a single-fraction treatment for bone pain has considerable advantages for both the patient and the radiotherapy department and it is important that its efficacy is properly evaluated. The treatment of bone pain should be distinguished from that of the complications of bone metastases such as cord compression and pathological fracture. On the basis of a large prospective randomised study at the Royal Marsden Hospital, we suggest that treatment with a single fraction of 8 Gy has an important role in the palliation of bone pain.

Yours, etc.,
P. PRICE
P. J. HOSKIN
J. R. YARNOLD

Radiotherapy Section,
The Royal Marsden Hospital,
Downs Road,
Sutton,
Surrey SM2 5PT
(Received February 1986)

REFERENCES

PRICE, P., HOSKIN, P. J., EASTON, D., AUSTIN, D., PALMER, S. G. & YARNOLD, J. R., 1986. Prospective randomised trial of single and multifraction radiotherapy schedules in the treatment of painful bony metastases. *Radiotherapy and Oncology* (in press).

SNEE, M. P. & VYRAMUTHU, N., 1985. Metastatic carcinoma from unknown primary site: the experience of a large oncology centre. *British Journal of Radiology, 58,* 1091–1095.

(Author's reply)

THE EDITOR—SIR,
Price et al point out the numerous difficulties in drawing firm conclusions from data abstracted retrospectively from case notes. Such difficulties are especially pronounced in assessing such a subjective end-point as pain control.

However, I can confirm that there was no significant difference in the proportion of patients of poor performance status which was given single-fraction treatment, compared with those patients given fractionated radiotherapy; 62% and 54% in each group being of poor performance status, respectively. As regards dose prescribed, all but one patient out of 29 given a single exposure received 1000 cGy or more and the majority (86%) given fractionated treatment received 2000–2250 cGy in five fractions. Nevertheless, I cannot disprove the contention that other factors rather than the dose prescribed accounted for the differing response rates between the two groups. We fully accept that the data produced by a prospective randomised study, such as that performed by Price et al, are more reliable than those produced from a retrospective survey.

However, a recent reanalysis of the large Radiation Therapy Oncology Group study on the palliation of bone metastases does suggest there is a dose–response relationship in pain control when both subjective response and analgesic consumption are taken into consideration (Blitzer, 1985). This study unfortunately did not have a single fraction as a treatment option. We therefore await with interest the detailed results of the Marsden study.

Yours, etc.
M. P. SNEE

Glasgow Institute of Radiotherapeutics and Oncology,
Western Infirmary,
Glasgow G11 6NT
(Received March 1986)

REFERENCE

BLITZER, P., 1985. Reanalysis of the RTOG study of the palliation of symptomatic osseous metastasis. *Cancer, 55,* 1468–1472.

The radiation dose to an infant following maternal radiopharmaceutical administration

THE EDITOR—SIR,
Recommendations for interrupting breast feeding following maternal radiopharmaceutical administration have to be based on measurements of the excretion of radioactivity in human breast milk (Ahlgren et al, 1985; Coakley & Mountford, 1985). Following an ^{111}In-labelled leucocyte scan (ILLS), Butt and Szaz (1986) found from two measurements of breast milk radioactivity that the concentration of ^{111}In at 20 h after re-injection was greater than the concentration of activity at 6 h. Their low concentrations of activity were similar to our own earlier measurements of ^{111}In in breast milk following an ILLS

TABLE I

ABSORBED DOSE (CCAD) TO AN INFANT CUDDLED FOR 20 MIN IN EVERY HOUR ASSUMING THE DOSE-RATE WAS AT A MAXIMUM IMMEDIATELY AFTER INJECTION WHEN CUDDLING WAS STARTED (TAKEN FROM MOUNTFORD & COAKLEY, 1986)

Scan	Administered activity (MBq)	Compound	Absorbed dose (mGy)*		
			Right breast	Midline (navel)	Left breast
Brain	550	^{99}Tc^{m}-gluconate	0.42	0.32	0.52
Lung	37	^{99}Tc^{m}-DTPA (aerosol)	0.05	0.04	0.08
	75	^{99}Tc^{m}-MAA			
Bone	550	^{99}Tc^{m}-medronate	0.26	0.23	0.25
Leucocyte	14	^{111}In-leucocytes	2.10	0.40	1.37

*At these sites on a mother's skin surface.

(Mountford & Coakley, 1985). In addition, our study showed that the activity concentration peaked at about 12 h after re-injection and, thereafter, decayed monoexponentially with an effective half-life of 82 h. We also agree with their conclusion that, for uninterrupted feeding, the total activity ingested by an infant would be considerably less than one-tenth of the annual limit of intake for a newborn infant.

However, when an infant is held in close contact by its mother after radiopharmaceutical administration, it will also be exposed to radiation emitted from radioactivity retained by the mother. We have made some preliminary estimates of the potential close-contact absorbed dose (CCAD) received by an infant due to cuddling, by exposing some LiB thermoluminescent dosemeters (TLD) at three different sites on the surface of four female patients (Table I). These sites corresponded approximately to the position of the head and lower limbs of an infant while being cuddled. The method used to derive the CCAD from the TLD exposures is given in detail elsewhere (Mountford & Coakley, 1986). The values of CCAD given in Table I assumed that cuddling was resumed immediately after injection, that the infant was held in close contact for 20 min at the start of each hour, and that the surface dose-rate decayed at the same rate as the radionuclide's physical decay constant.

The anatomical distribution of CCAD was dependent on the radiopharmaceutical administered and its redistribution with time. The CCAD for a ^{99}Tc^{m} lung scan was much less than the ingested dose from radioactivity excreted in breast milk for uninterrupted feeding (Ahlgren et al, 1985). The CCAD for a ^{99}Tc^{m} bone scan exceeded the ingestion dose (Ahlgren et al, 1985), but was only 5% of the dose-equivalent limit for a member of the public. There are no published data describing the excretion of radioactivity in breast milk following injection of ^{99}Tc^{m}-gluconate. However, measurements following injection of another renal agent, ^{99}Tc^{m}-DTPA, have shown a very low excretion in breast milk (Ahlgren et al, 1985; Mountford et al, 1985), so the CCAD estimated for a gluconate brain scan will probably exceed the ingested dose. Although the ingested doses from the latter two types of ^{99}Tc^{m} scans are very low for uninterrupted feeding, we normally recommend an interruption to feeding of 4 h in order to provide some reassurance to the mother (Coakley & Mountford, 1985). A similar interruption to cuddling during this period will decrease the CCAD by 35%.

Despite its low administered activity (14 MBq), the ILLS produced the greatest CCAD, with the value for the right breast site being 40% of the limit for a member of the public. Therefore, although the ingested activity after an ILLS does not warrant interruption, we consider that close contact between mother and infant should be restricted. If, as before, breast feeding was resumed at 4 h after reinjection of ^{111}In-leucocytes, then advising the mother to cuddle her infant only at feeding times (*i.e.* 20 min every 4 h) for the first 3 days after re-injection will reduce the CCAD by about 40%.

Finally, it is stressed that an infant will still receive a radiation dose from cuddling even if the mother is not breast feeding her infant.

We are grateful to Mr B. F. Wall of the National Radiological Protection Board for reading the TLD.

Yours, etc.,
P. J. MOUNTFORD
A. J. COAKLEY

Department of Nuclear Medicine,
Kent and Canterbury Hospital,
Ethelbert Road,
Canterbury,
Kent CT1 3NG

(*Received March 1986*)

REFERENCES

AHLGREN, L., IVARSSON, S., JOHANSSON, L., MATTSON, S. & NOSSLIN, B., 1985. Excretion of radionuclides after the administration of radiopharmaceuticals. *Journal of Nuclear Medicine, 26*, 1085–1090.

BUTT, D. & SZAZ, K. F., 1986. Indium-111 radioactivity in breast milk. *British Journal of Radiology, 59*, 80.

COAKLEY, A. J. & MOUNTFORD, P. J., 1985. Nuclear medicine and the nursing mother. *British Medical Journal, 291*, 159–160.

MOUNTFORD, P. J. & COAKLEY, A. J., 1985. Excretion of radioactivity in breast milk after an indium-111 leucocyte scan. *Journal of Nuclear Medicine, 26*, 1096–1097.

MOUNTFORD, P. J. & COAKLEY, A. J., 1986. Radiopharmaceuticals in breast milk. In: *Proceedings of the Fourth International Radiopharmaceutical Dosimetry Symposium*. Ed. by A. Schlafke-Stelson & E. E. Watson (Oak Ridge Associated Universities, Oak Ridge, Tennessee), in press.

MOUNTFORD, P. J., COAKLEY, A. J. & HALL, F. M., 1985. Excretion of radioactivity in breast milk following injection of Tc-99m DTPA. *Nuclear Medicine Communications, 6*, 341–345.

1986, *The British Journal of Radiology*, 59, 959–960 SEPTEMBER 1986

Correspondence

Ultrasound of the hip in childhood

THE EDITOR—SIR,

We read with interest two articles (Adam et al, 1986; Peck, 1986) on the subject of ultrasound of the hip in childhood. We are pleased to see that others consider this technique of value and that their findings agree broadly with those that we described in January 1984 (Wilson et al, 1984). We are pleased to see that both articles now document our impression that the plain-film signs of effusion are very inaccurate and that ultrasound findings correlate well with that of diagnostic aspiration. We note that both papers describe the technique of scanning in a plane parallel to the femoral neck to detect displacement of the anterior capsule without acknowledging that this is identical to the method that we described in 1984.

Dr Peck describes irregularity of the femoral head (indicated by an arrow in Fig. 4 of his article) indicating that this is a sign of Perthes' disease. In fact the structure indicated is the irregular bony contour of ossification in the femoral capital epiphysis which is deep to the cartilaginous coating of the femoral head. We have also observed this type of irregularity in normal epiphyses and it does not necessarily indicate osteonecrosis. Arthrography may well demonstrate an intact cartilage. In answer to the question regarding Perthes' disease we have seen a number of patients in our 4 years of practice with this technique who presented with an irritable hip, demonstrated an effusion on ultrasound and later developed the radiological changes of Perthes' disease.

Although we are delighted to see publications on the subject of ultrasound of the hip, we would prefer to see authors tackling new aspects of the subject.

Yours, etc.,
D. J. WILSON
D. J. GREEN

The Nuffield Orthopaedic Centre,
Headington,
Oxford OX3 7LD
(*Received April 1986*)

REFERENCES

ADAM, R., HENDRY, G. M. A., MOSS, J., WILD, S. R. & GILLESPIE, I., 1986. Arthrosonography of the irritable hip in childhood: a review of 1 year's experience. *British Journal of Radiology*, 59, 205–208.

PECK, R. J., 1986. Ultrasound of the painful hip in children. *British Journal of Radiology*, 59, 293–294.

WILSON, D. J., GREEN, D. J. & MACLARNON, J. C., 1984. Arthrosonography of the painful hip. *Clinical Radiology*, 35, 17–19.

Economics of xenon 127, xenon 133 and krypton 81m for routine ventilation imaging of the lungs

THE EDITOR—SIR,

In response to the letter from Nimmo et al (1986), perhaps we might briefly make two points.

(i) Steady-state $^{81}Kr^m$ does reflect regional ventilation at normal and low ventilatory turnover where there is a straight-line relationship between $^{81}Kr^m$ signal and ventilation (Fazio & Jones, 1975). At higher specific ventilation, the relationship is less linear but surely that does not matter. It is regional decreased ventilation you are looking for.

(ii) Only 15–20% of patients referred for lung scans will have pulmonary embolic disease. Most of the remainder will have evidence of acute or chronic lung disease often not visible on the chest radiograph. Are we to abandon this population of patients or try to assess the nature and severity of their lung disease? When we do bone scans we do not ignore abnormalities simply because they are not due to metastatic disease. Why in lung scans should we adopt so limited an approach to the study of lung disease? To study regional lung function, one needs both ventilation and perfusion images. There should be multiple images and they should be comparable.

Yours, etc.,
J. P. FINN
J. P. LAVENDER

Royal Postgraduate Medical School,
Hammersmith Hospital,
London W12 0HS
(*Received April 1986*)

REFERENCES

FAZIO, F. & JONES, T., 1975. Assessment of regional ventilation by continuous inhalation of radioactive krypton 81m. *British Medical Journal*, *iii*, 673–676.

NIMMO, M. J., MERRICK, M. V. & MILLAR, A. M., 1986. Economics of xenon 127, xenon 133 and krypton 81m for routine ventilation imaging of the lungs. *British Journal of Radiology*, 59, 298–299.

Acute focal bacterial nephritis

THE EDITOR—SIR,

Following the paper by McKinstry (1985) on acute lobar nephronia in children, we can add three further paediatric case reports of acute focal bacterial nephritis (AFBN), a descriptive term which we prefer. Two of these may be found in a publication to which reference is made in one of the papers (Rosenfield et al, 1979) cited by the author, while the other case was reported by us (Lawson et al, 1985).

Lebowitz et al (1977) report two children, one of whom had no vesico-ureteric reflux (VUR) on micturating cystourethrography (MCU), while the other had VUR and severe pelviureteric junction (PUJ) obstruction in the kidney with AFBN. These were said to be illustrative examples and the paper suggested that most children with renal parenchymal infection do not have an underlying renal tract abnormality, but are either completely well or have a minor, remote focus of infection. Unfortunately this classification was not substantiated by the age or numbers of subjects who had been studied, nor by the investigations carried out upon them, and so its validity cannot be confirmed. Permission for micturating cystography was not granted for our patient (Lawson et al, 1985).

In contrast to the above hypothesis, others have suggested VUR as being important in the pathogenesis of AFBN in children. The clinical evidence supporting this comes from five published reports, summarised in Table I.

Of the 10 case reports, six children had VUR but one of these also had a severe PUJ obstruction and another an ileal-loop diversion. One child was shown to have no reflux, while the remaining three children (of whom one was a 17-year-old diabetic) did not have MCU. It is known that girls have three times as many urinary tract infections as boys and yet the sex

TABLE I

Author	Sex	Age (years)	ABFN affected kidney	Result of MCU	Other abnormalities
Lebowitz	M	7	Right	No reflux	
Lebowitz	M	10	Right	Right-sided VUR	Right-sided severe PUJ obstruction
Rosenfield	?	14/52	?	One of these children had bilateral VUR —the other did not have MCU	
Rosenfield	?	?	?		
Siegel	F	8½	Right	Right-sided VUR	Reflux from ileal-loop diversion
Siegel	F	6	Right	Right-sided VUR	
Siegel	F	5	Right	Right-sided VUR	
Siegel	F	17	Left	Not done	Diabetic
Lawson	M	$1\frac{7}{12}$	Right	Not done	
McKinstry	M	3	Right	Bilateral VUR	

incidence in eight cases was equal. This would support the theory that there is probably an underlying abnormality, such as VUR, which must be present with infected urine before parenchymal infection occurs. We agree with Dr McKinstry that MCU should be performed to select those who need prophylactic antibiotic treatment as well as giving further evidence in determining the pathogenesis of this disease.

We were interested by Dr McKinstry's negative computed tomography (CT) findings, particularly as Hoddick et al (1983) have found this a more sensitive investigation. Dr McKinstry does not state whether intravenous contrast medium was given and we wonder whether the CT was negative for this reason In our case CT was done to investigate the possibility of a tumour and was invaluable when post-contrast scans showed a wedge-shaped defect involving both cortex and medulla, characteristic of AFBN. Nevertheless we agree that ultrasound is the initial investigation of choice although it would appear insensitive in the detection of scarring.

Yours, etc.,
G. R. LAWSON
*F E WHITE
†J E S SCOTT

Department of Child Health,
University of Newcastle-upon-Tyne,
*Department of Radiology,
Newcastle General Hospital and
†Department of Surgery,
University of Newcastle-upon-Tyne
(*Received March 1986*)

REFERENCES

HODDICK, W., JEFFREY, R. B., GOLDBERG, H. I., FEDERLE, M P. & LAING, F. C., 1983. CT and sonography of severe renal and perirenal infections. *American Journal of Roentgenology, 140,* 517–520.

LAWSON, G R, WHITE, F. E & ALEXANDER, F W., 1985. Acute focal bacterial nephritis. *Archives of Disease in Childhood, 60,* 475–477

LEBOWITZ, R. L., FELLOWS, K. E. & COLODNY, A. H, 1977. Renal parenchymal infections in children *Radiologic Clinics of North America, 15,* 37–47

MCKINSTRY, C. S., 1985 Acute lobar nephronia *British Journal of Radiology, 58,* 1217–1219.

ROSENFIELD, A. T, GLICKMAN, M. G., TAYLOR, K J. W., CRADE, M & HODSON, J., 1979. Acute focal bacterial nephritis (acute lobar nephronia). *Radiology, 132,* 553–561.

SIEGEL, M. J. & GLASIER, C. M, 1981 Acute focal bacterial nephritis, in children significance of ureteral reflux. *American Journal of Roentgenology, 137,* 257–260.

(*Author's reply*)

THE EDITOR—SIR,

I would like to thank Drs Lawson, White and Scott for their interest and for drawing attention to the three further reports of acute lobar nephronia (ALN) in the literature, including their own recent case

In the case which I described, CT was performed without contrast. It was felt that repeating it with contrast was not justified, since the plain scan had excluded a tumour by demonstrating obvious resolution of the upper-pole swelling, seen on ultrasound However, I agree that a post-contrast study might well have shown changes indicative of ALN.

Yours, etc.
C. S. MCKINSTRY

Department of Radiology,
Royal Victoria Hospital,
Belfast BT12 6BA
(*Received April 1986*)

Conversazione

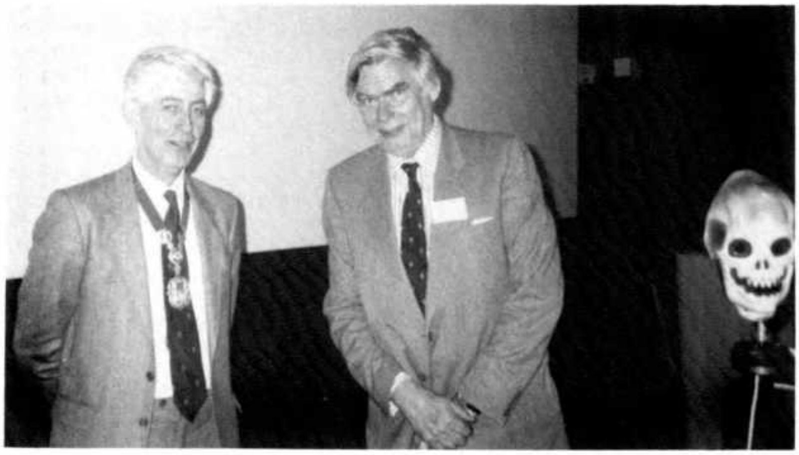
The 1986 Conversazione, the annual occasion for Institute members and their families, staff and friends to enjoy both science and supper together, was held on June 19 in the beautiful surroundings of the newly rebuilt Royal Society of Medicine. Over 100 people attended and generous support was given by AXrEM and Kodak.

The evening began with a sherry reception in the sunlit atrium before guests moved on to the lecture theatre where Professor Peter Wells presided over the proceedings.

Professor Ian Isherwood introduced "The many worlds of Britain", an audio-visual spectacular based upon the presentation of the British Radiology Delegation to the International Society of Radiology in Honolulu last year, in support of its bid to bring the International Congress of Radiology to Britain in 1989.

Richard Gregory, Professor in Neuropsychology and Head of the Brain and Perception Laboratory at the University of Bristol, gave the BIR Silvanus Thompson Memorial Lecture, "Seeing through illusion". This fascinating examination of the physiology and psychology of vision was not, as Professor Gregory said, "radiology". It did, however, touch meaningfully upon imaging and, in particular, the perception of images. The full text of the lecture will be published in the *British Journal of Radiology*.

Following the lecture, Professor Wells presented the BIR Awards for 1986: the Barclay Medal to Dr D. K. Bewley, the Röntgen Prize to Professor N. M. Bleehen and the Barclay Prize to Professor M. N. Maisey. The evening was pleasantly prolonged with a wine and buffet supper.



Professor Wells (left), Professor Gregory and an illusion.

Obituary

Professor Harold A. B. Simons, M.A., Ph.D., F.Inst.P.

The sudden death of Harold Simons on February 13, 1986 brought to an untimely end one of the pioneers of physics in medicine in this country.

For more than three decades he was an influential figure in academic circles and at the Royal Free Hospital School of Medicine. He believed passionately in the educational value of physics, and his views on the need to equip doctors for the increasing use of technology in medicine were ahead of their time. Alone among the teachers in the London medical schools he managed to secure a place beyond the closure of the first M.B. course at his own school for the continued teaching of physics as a distinct discipline in the pre-clinical curriculum.

Following his father's distinguished academic career in physics, Harold Simons studied with the elite at the Cavendish Laboratory, Cambridge. On graduation he contributed his expertise to the war effort as a scientific officer with the Admiralty. As for so many others, this period provided a wealth of experience and he was fond of recalling incidents with wry humour, such as when a torpedo he was testing landed high and dry on a Scottish beach. After the war he returned to academic life as a lecturer and research fellow at St Bartholomew's, and then in 1952 he was appointed Reader to take charge of the physics department at the Royal Free. Ten years later he was appointed to a personal Chair in Physics as Applied to Medicine. The title of Emeritus Professor was conferred on him on his retirement in 1983.

Harold Simons' interest in the practical applications of physics to medicine were consistently maintained. He was closely involved in the work of his staff and postgraduate students. His own research interests in the field of radiation physics led to notable publications on a variety of topics, including the design of collimators for scanning and solid-state detectors for proton microdosimetry. For 5 years he was Honorary Editor of *Physics in Medicine and Biology* and led the journal through a period of rapid expansion in scope and importance.

In later years he devoted much of his time and effort to administrative matters in department, school and university. The move from the old buildings in Hunter Street to the new hospital site in Hampstead coincided with the establishment of new organisational arrangements within the school, and the introduction of a new M.B.B.S. curriculum. His insight into technical and financial aspects during the years of planning resulted in substantial benefits to all involved. He recognised the importance for education of close-circuit television and computing, and established appropriate services at Hampstead. Computing was introduced at an early stage to the curriculum. Shortly before his retirement, in his position as Chairman of the Board of Studies, he led the successful campaign for the retention of radiobiology as a discipline within the university against the very real threat of extinction arising from the effects of the financial cuts imposed by the University Grants Committee. Although recently elected back onto the school council to assist in guiding the fortunes of the Royal Free, his untimely death sadly prevented him from serving.

Harold Simons' clarity of thought, "no-nonsense" approach and integrity were much valued by all who knew him. Many will miss him as a friend.

M. F. Cottrall

Notices

The death of Dr Curt Westman

Sadly, Dr Curt Westman, an Honorary Member of and great friend to the Institute, died on July 11, in Stockholm. He said before his death that he would make arrangements for the visits of British radiologists to his clinic in Stockholm to continue. An obituary, by Professor Isherwood, will be published in a forthcoming issue of the *Bulletin*.

The Marii Sklodowskeij-Curie Medal

Professor J. F. Fowler, Director of the Gray Laboratory, Northwood, Middlesex, has been awarded the 6th Marii Sklodowskeij-Curie Medal by the Polish Society for Radiation Research.

The presentation took place in the 14th century Collegium Maius of the Jagiellonian University, Krakow, on June 12, 1986. The medal was established in 1980 and previous award winners include Professors Kroh and Rudnioki from Poland, Lord Dainton from the UK and Professor Pikaev from the USSR.

XIV Symposium Neuroradiologicum

Professor George du Boulay C.B.E. has been chosen to be President of the XIV Symposium Neuroradiologicum. This will take place in London, at the Queen Elizabeth II Conference Centre in 1990.

The series of Symposia Neuroradiologica began in 1939 and, apart from during the War, has been held about every 4 years. The XIII Symposium Neuroradiologicum took place under the Presidency of Professor Torgny Greitz in Stockholm, June 23–28 this year. Symposium Neuroradiologicum has been to Britain once before, in 1955, under the Presidency of Dr James Bull.

Although the XIV Symposium Neuroradiologicum will be held in London, Professor du Boulay hopes that all the neuroradiologists of the British Isles and Eire will feel it belongs to them to be hosts to the rest of the world.

The NPL Research Associate Scheme

The Research Associate Scheme (RAS) is designed to enable scientists and engineers from industry, research associations, higher education institutions and other organisations to work at the National Physical Laboratory (NPL) on projects of mutual benefit to the Laboratory and their employer. Transfer of technology is achieved through the close co-operation that develops between the parties involved which, it is hoped, will continue on an informal basis after the Associateship has ended. Suitable training packages are also laid on by the Laboratory as an essential part of each Associateship.

The RAS is open to scientists and engineers from organisations who have the ability to contribute to the work programmes and to benefit from a period spent at the NPL. Associates remain (or become) employees of NPL's partner organisations and continue to receive their normal salaries and retain their pension rights etc. In many cases NPL will be able to make a contribution to the employers towards the Associates' salaries and other approved expenses such as travelling costs. Each case will be judged on its merits and the percentage of costs paid by NPL will reflect the expected balance of benefits between the Laboratory and the partner organisation.

The normal period of association will be from 6 months to 3 years, a period sufficient to allow a real contribution to be made to a project. Periods outside this duration can be considered in exceptional cases. During the appointment the Associate will normally be expected to spend at least 90% of his working time at NPL. The projects undertaken will be related to NPL's normal work programme, which covers a broad range of topics encompassing all aspects of measurement and standards including radiation dosimetry and medical ultrasound.

For further information please contact. The Deputy Secretary, National Physical Laboratory, Queens Road, Teddington, Middlesex TW11 0LW (Tel 01-943 6019).

Draft Code of Practice on Exposure to Radon: Part 3 of the Approved Code of Practice (Ionising Radiations Regulations 1985)

A draft of Part 3 of the Approved Code of Practice for the protection of persons against ionising radiation arising from any work activity, covering exposure to radon, has been published in a consultative document by the Health and Safety Commission.

The Ionising Radiations Regulations 1985 and Parts 1 and 2 of the Approved Code of Practice were published in September 1985 The introduction to the Code stated that there would be a third part, containing guidance on the application of the regulations to work involving increased exposure to isotopes of radon and their decay products Part 3 has been drawn up following consultation with interested parties and in particular with a working group comprising nominees from the Confederation of British Industry, Trades Union Congress and the National Radiological Protection Board, together with independent experts and representatives of the Health and Safety Executive.

The consultative document has been sent direct to all known interested parties. Copies of the document are also available, free of charge, from. Health and Safety Executive, Nuclear Policy Branch, Radiation Protection Section, Room 373, Baynards House, 1 Chepstow Place, London W2 4TF (Tel. 01-229 3456 ext. 6115/6116)

Press release

New Du Pont "Micro Radiology Manager" in line with Körner Report

"The main task of those who guide and manage the provision of health care is to ensure quality, maintain costs and secure access to those who need it Or, to put it more simply, to provide a good service for as many people as need it at least cost" This was the opening paragraph of the report of the Steering Group on Health Services Information under the chairmanship of Mrs Edith Korner, which reported in 1982 Management can only be effective and efficient if it is based in sound statistics; many areas of the NHS, however, fail to use the available data properly, analyse it appropriately or present it informatively

In light of this, in 1980 the DHSS set up a Korner Steering Group with these terms of reference. to agree, implement and keep under review principles and procedures to guide the future development of health-services information systems; to identify and resolve health-services information issues requiring a co-ordinated approach, to review existing health-services information systems; and to consider proposals for changes to, or developments in, health-services information systems arising elsewhere and, if acceptable, to assess priorities for their development and implementation.

The Körner report criticised the current system of data collection on X-ray services in the following terms. Although each of the 200 possible radiological examinations is at present given a value in units based on the time it takes and the staff involved, the reported total number of units gives no indication of the procedures performed. Since the unit system is based on staff time, it gives no indication of resources used. The activity of the department is not analysed in terms of the clinical initiator of the request for example, do surgical departments need different radiographs from casualty wards? There is no link between data about radiological activity and other clinical data either in the hospital or locally

Korner therefore recommended a number of changes, to take effect from April 1987, in the way data are collected and analysed, including the suggestion that radiological examinations be divided into six groups based on costs, and that the number of requests for examinations in each of these areas be recorded It was also recommended that a national vocabulary of diagnostic services be established, so that each procedure can be assigned a code number, identifying it uniquely

This will enable local managers both to interpret the statistical data and to allocate resources accordingly. Thus a department will be able to justify its budget, or an increase in it, on the basis of the work it actually performs It will also allow the implementation of cross-budgeting, where the radiology department charges other clinical specialities a realistic cost for procedures initiated at its request Diagnostic facilities can be planned and forecast on the basis of the clinical activity in other areas of the hospital or local medical services.

Du Pont's "Micro Radiology Manager" (MRM), an integrated software/hardware management system with proven local area network (LAN) technology, is the result of collaboration between Du Pont and Trinity Computing Systems of Houston. It is designed so that from first registering with the radiology department, a patient's characteristics and records move electronically through the system with him. The film packets are tagged by bar codes, ensuring that they are subsequently easier to access and less likely to be misplaced.

"MRM" includes modules which assess quality control and performance indices, so that the radiology department manager can identify areas of waste or under-resourcing and make the appropriate modifications to practice or procedure.

In computer terms, "MRM" is a LAN based on the proven computer technology combining the advantages of intelligent terminals with those of a distributed system, but without the drawbacks of time-sharing on a central minicomputer. Any IBM-compatible program can be run on individual workstations without reference to the central file server, except for retrieval of data. The system is secured by a hierarchy of passwords which ensures confidentiality of patient records.

The advantages of "MRM" are not only better departmental management and ease of reporting statistics, case-report writing and data handling, but also enhanced patient care and improved cost-efficiency.

In line with Du Pont's stated commitment to customer education and support, full training and software/hardware support are available to purchasers of Du Pont's "Micro Radiology Manager" For further information please contact: Denise Craig, Du Pont (UK) Ltd, Wedgewood Way, Stevenage, Hertfordshire SG1 4QN (Tel. 0483-734 000) or Julie Cracknell, Burson-Marsteller, 25 North Row, London W1R 2BY (Tel. 01-499 0414).

Library news

The BIR Library is open weekdays 9 a.m.–5 p.m. (7 p.m. on Thursdays)

The Librarian, Mrs Gunnel Ingham, is in attendance Tuesdays 11 a.m–5 p m, and Thursdays 11 a.m.–7 p m., and Mrs Angela Lansdown, daily 9 a m–5 p m. (Tel. 01-580 4085).

The journal stock includes more than 100 titles Though journals may not be taken out of the library, there is a photocopy service, also available by post. A list of current journals is available on request and is also published in the March and September issues of the Bulletin

Most books (excepting the historical collection) are available on loan.

Recent additions to the Library

Anbar, M., Spangler, R. A. & Scott, P. (Eds): Clinical biophysics. 1985
Burgener, F A & Kormano, M.: Differential diagnosis in conventional radiology. 1985
Engel, J M, Flesch, U. & Stuttgen, G (Eds). Thermological methods. 1985
Hufton, A. P (Ed). Practical aspects of thermoluminescence dosimetry 1985
Kalifa, G.: Pediatric ultrasonography 1986
Latchaw, R E.: Computed tomography of the head, neck and spine. 1985
Ryo, U Y., Bekerman, C. & Pinsky, S. M · Atlas of nuclear medicine artifacts and variants. 1985
Spindola-Franco, H. & Fish, B. G. Radiology of the heart. 1985
Van Mill, G J., Moulaert, A J & Harinck, E Atlas of two-dimensional echocardiography in congenital cardiac defects 1985
Walsh, J. W. (Ed): Computed tomography of the pelvis. 1985
Zoetelief, J., Broerse, J. J. & Davies, R. W.: Radiation protection (protocol for X-ray dosimetry). 1985

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Acta Radiologica—Oncology
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Applied Health Physics, Abstracts and Notes
Applied Radiation and Isotopes
Astro Newsletter
Australasian Radiology
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British Journal of.Cancer
British Journal of Radiology
British Medical Bulletin
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Cancer
Cancer Research
Cancer Research Campaign Annual Report
Cancer Treatment Reviews
Cardiovascular and Interventional Radiology
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Chinese Journal of Nuclear Medicine
Chinese Journal of Radiology
Clinical Nuclear Medicine
(Clinical Oncology: cont as European Journal of Surgical Oncology)
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Clinical Radiology
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Current Opinion in Cardiology
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Deutsche Roentgengesellschaft Informationen
Diagnostic Imaging (USA)
European Journal of Cancer and Clinical Oncology
European Journal of Nuclear Medicine
European Journal of Radiology
European Journal of Surgical Oncology
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Fortschritte auf dem Gebiete der Roentgenstrahlen
Gastrointestinal Radiology
Health Physics
HPA Bulletin
ISRRT Newsletter
Indian Journal of Radiology
International Agency for Research on Cancer. Annual Report
International Atomic Energy Agency Bulletin
International Journal of Hyperthermia
International Journal of Radiation Biology
International Journal of Radiation Oncology, Biology, Physics
Investigative Radiology
Japanese Journal of Nuclear Medicine
Journal Belge de Radiologie
Journal de Radiologie (France)
Journal Européen de Radiotherapie
Journal of Clinical Oncology
Journal of Clinical Ultrasound
Journal of Computed Tomography
Journal of Computer Assisted Tomography
Journal of Nuclear Medicine
Journal of the Canadian Association of Radiologists
Journal of The National Cancer Institute
Journal of The Royal Society of Medicine
Journal of The Society for Radiological Protection
Journal of X-ray Technology
Lancet
Magnetic Resonance in Medicine
Medical Physics
Medical Radiography and Photography
Medicamundi
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Neuroradiology
Nuclear Medicine and Biology
Nuclear Medicine Communications
Oncologia (Rumania)
Pediatric Radiology
Physics in Medicine and Biology
Proceedings of The American Association for Cancer Research
Proceedings of the American Society of Clinical Oncology
Rad
Radiation Protection Dosimetry
Radiation Research
Radiatsionnaya Biologiya (USSR)
Radiographics
Radiography
Radiography News
Radiologia Medica (Italy)
Radiologic Clinics of North America
Radiological Protection Bulletin
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Seminars in Roentgenology
Seminars in Ultrasound
Skeletal Radiology
Strahlentherapie
Ultrasonic Imaging
Ultrasonics
Ultrasound in Medicine and Biology
Urologic Radiology
World Health
Yearbook of Diagnostic Radiology

BIR calendar events

Unless otherwise indicated, enquiries about the following events should be addressed to the Assistant Secretary: Programme, British Institute of Radiology, 36 Portland Place, London W1N 3DG (Tel. 01-580 4085).

The meetings are at 36 Portland Place unless otherwise stated. Attendance is open to non-members.

Joint RCR/BIR/RSM Autumn Provincial Meeting; RCR Annual General Meeting

September 11–13, 1986
Sheffield
Organised by the RCR. Further details from the Meetings Secretary, The Royal College of Radiologists, 38 Portland Place, London W1N 3PG (Tel. 01-636 4432/3).

Regulations and Guidance on Radiation Protection: a seminar

October 2, 1986 at 10 a.m.
Middlesex Hospital Medical School, London W1
Chairmen: Professor R. J. Berry and Mrs J. Barrett.
Speakers: Mr P. Beaver, Dr J. Gill, Mr R. Grix, Mr I. Hendra, Mr B. Godfrey, Mr P. Richardson, Mr B. Aves, Dr L. K. Harding, Dr P. Roberts and Dr J. G. Russell.
Joint BIR/COR meeting.

Interventional Radiology of the Spine

October 16, 1986 at 5.45 p.m.
Chairman: Dr J. C. MacLarnon.
Speakers: Dr D. J. Stoker, Dr B. E. Kendall, Dr I. W. McCall and Dr E. Colhoun.

Accelerated Fractionation and Hyperfractionation: experimental and clinical

November 14, 1986 at 11 a.m.
Organised by the Radiobiology Subcommittee. To conclude with the Silvanus Thompson Memorial Lecture: "Cancer—the failure of treatment" by Dr R. H. Thomlinson.

Diagnostic and Therapeutic Uses of Radioisotopes in Oncology

November 26, 1986 at 10.30 a.m.
All day meeting organised by Nuclear Medicine Subcommittee.
Chairmen: Professor R. J. Berry and Dr R. T. D. Oliver. Speakers: Dr I. Fogelman, Dr A. Laing, Dr D. M. Ackery, Dr N. W. Garvie, Dr K. E. Britton, Dr A. Epenetos, Dr S. Clarke, Dr P. N. Plowman and Dr V. R. McCready.

Practical Aspects of Magnetic Resonance Imaging

January 14, 1987
Middlesex Hospital Medical School, London
Joint BIR/RCR meeting.

Uroradiology Update

January 15, 1987 at 5.30 p.m.
Chairman: Dr D. Rickards. Speakers: Dr D. Rickards, Dr J. Pemberton, Dr C. E. L. Freer, Mr G. Watson, Dr R. Johnson, Dr W. Lees, Professor D. J. Allison.
Joint BIR/RCR/RSM meeting.

Radionuclide Investigations of the Lung

February 11, 1987
Joint IPSM/BIR (Nuclear Medicine Subcommittee) all day meeting organised by IPSM.

All day non-topic proffered papers meeting

February 13, 1987
Joint ARR/BIR (Radiobiology Subcommittee) meeting organised by the Association for Radiation Research.

Picture Archiving and Communications Systems

February 25, 1987
Venue to be announced
Chairman: Professor I. Isherwood.
Topics will include image display, image transmission and image storage.
All day meeting organised by Industry Committee.

Annual General Meeting

May 14, 1987 at 4.30 p.m.

Advance Notice

British Institute of Radiology 45th Annual Congress, incorporating the joint BIR/RCR/RSM (Section of Radiology) spring meeting

RADIOLOGY '87

University of Southampton
April 1–3, 1987

The Congress will cover all aspects of radiology—X-ray diagnosis, radiotherapy, radiation oncology, nuclear medicine, ultrasound, NMR, radiological physics, radiobiology, radiation protection and related disciplines and is expected to include:

The BIR Mackenzie Davidson Memorial Lecture, by Professor M. J. Peckham, "The clinical biology of testicular germ cell tumours"
The BIR Mayneord Lecture (sponsored by 3M UK plc), by Dr Frances Fry
The RCR George Simon Lecture, by Dr J. C. Batten
The BIR Presidential Address, by Professor R. J. Berry

The BIR Annual Dinner will be held at the Polygon Hotel, Southampton, on April 2.

Proffered papers are invited. Please apply for form from the BIR. Absolute closing date for receipt of completed proffered paper forms is November 30, 1986.

For further information please apply to the Assistant Secretary: Programme, The British Institute of Radiology, 36 Portland Place, London W1N 3DG (Tel. 01-580-4085).

Imaging in Radiotherapy

May 15, 1987
Chairmen: Dr D. Thwaites and another to be announced.
Joint IPSM/BIR all day meeting organised by IPSM.

Dysphagia

May 20, 1987
Royal Society of Medicine, London
Joint RSM/RCR/BIR all day meeting to be organised by the RSM.

Conversazione

May 20, 1987
Royal Naval College, Greenwich

Meetings and courses

As a service to our readers, the title, date and place of meetings and contact address will be inserted free of charge: any additional information will be charged at £1.75 per printed line, per insertion. Please contact the Managing Editor.

Assessing and Managing Health and Environmental Risks from Energy and Other Complex Industrial Systems
October 13–17, 1986
Paris
Further details: M. Pankhurst, Department of Energy, Atomic Energy Division, Thames House South, Millbank, London SW1P 4QJ (Tel. 01-211 6850).

Diagnostic Radiology Seminars
November 3–7, 1986
Maui, Hawaii
January 19–23, 1987
Ixtapa, Mexico
February 1–6, 1987
Aspen, Colorado
February 22–27, 1987
Park City, Utah
Further details: Radiology Postgraduate Education, University of California, Third and Parnassus Avenues, Room C324, San Francisco, CA 94143, USA (Tel. 415-476 5731).

The Biological Effects of Ionising Radiation
November 24–25, 1986
Royal Postgraduate Medical School, Hammersmith Hospital, London
Further details: Dr Gari Donn, 8 Buckingham Road, Brighton, East Sussex BN1 3RA (Tel. 0273-202516).

The British Medical Ultrasound Society 18th Annual Scientific Meeting
December 16–18, 1986
University of Warwick, Coventry
Further details: Mrs L. Blench, General Secretary, BMUS, 36 Portland Place, London W1N 3DG (Tel. 01-636 3714).

Meeting of the International Working Party for the Diagnosis and Treatment of Carcinoma of the Cervix in Developing Areas
January 23–29, 1987
Calcutta
Further details: Dr Margaret Snelling, 7 Elm Place, London SW7 3QH.

2nd International Symposium on Magnetic Resonance Imaging: MR '87
January 29–February 1, 1987
Garmisch-Partenkirchen, West Germany
Further details: Sekretariat Professor Dr J. Lissner, Radiologische Klinik, Klinikum Grosshadern, Marchioninistr. 15, 8000 München 70, West Germany (Tel. 089-7095 2750).

Perspectives in Radioprotection
March 13–14, 1987
Bethesda, Maryland
Further details: Dr Joseph F. Weiss, Armed Forces Radiobiology Research Institute, Bethesda, MD 20814-5145, USA.

Diagnostic Imaging 1987
March 16–21, 1987
Kauai, Hawaii
Further details: Radiology Postgraduate Education, University of California, Third and Parnassus Avenues, Room C324, San Francisco, CA 94143, USA (Tel. 415-476 5731).

Intra-uterine Diagnosis and Treatment: the new frontier
April 2–4, 1987
San Diego, California
Further details: Office of CME, M-017, UC San Diego School of Medicine, La Jolla, CA 92093, USA (Tel. 619-534 3940).

British Nuclear Medicine Society Annual Congress
April 12–15, 1987
Imperial College, London
Further details: Mrs A. Taylor, BNMS Conference Secretary, 22 Leinster Avenue, East Sheen, London SW14 7JP.

The Finzi Lecture
April 15, 1987
Royal Society of Medicine, London
"The solitary pulmonary nodule" by Dr S. Segalmann.
Meeting to be organised by RSM.

College of Radiographers' Annual Conference
July 1–3, 1987
Scarborough
Further details: Miss C. Aldridge, College of Radiographers, 14 Upper Wimpole Street, London W1M 8BN (Tel. 01-935 5726, ext. 206).

Diagnostic Radiology Update
July 27–30, 1987
London
August 3–6, 1987
Paris, France
Further details: Ryals & Associates, PO Box 920113, Norcross, GA 30092-0113, USA (Tel. 404-641 9773).

Radiology Update in Scandinavia and the Soviet Union
August 8–19, 1987
Copenhagen, Stockholm and Leningrad
Further details: Ryals & Associates, PO Box 920113, Norcross, GA 30092-0113, USA (Tel. 404-641 9773).

3rd Annual Sonographers' Review Course
August 28–30, 1987
San Diego, California, USA
Further details: Ryals & Associates, PO Box 920113, Norcross, GA 30092-0113, USA (Tel. 404-641 9773).

Chest Imaging Conference 1987
August 31–September 2, 1987
University of Wisconsin, USA
Call for abstracts.
Further details: CIC-87 Program Committee, Department of Medical Physics, University of Wisconsin, 1300 University Avenue, Madison, WI 53706, USA (Tel. 608-262 2171).

Breast Disease Symposium
September 9–11, 1987
San Diego, California, USA
Further details: Ryals & Associates, PO Box 920113, Norcross, GA 30092-0113, USA (Tel. 404-641 9773).

San Diego Imaging Symposium
September 9–11, 1987
San Diego, California, USA
Further details: Ryals & Associates, PO Box 920113, Norcross, GA 30092-0113, USA (Tel. 404-641 9773).

HPA Annual General Meeting and IPSM Scientific Meeting
September 15–19, 1987
Liverpool
Further details: IPSM, 47 Belgrave Square, London SW1X 8QX (Tel. 01-235 6111).

7th International Congress of the International Radiation Protection Association: radiation protection practice
April 10–17, 1988
Sydney, Australia
Further details: IRPA 7 Secretariat, GPO Box 2609, Sydney, NSW 2001, Australia (Tel. 02-241 1478, Telex AA74845 "Consec", Cable "Convention" Sydney).

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☐ 18. **Quality Assurance** Criteria and methods for quality assurance in medical X-ray diagnosis 1984 £16.00

☐ 19. **Radiation Damage to Skin** Fundamentals and Practical Aspects 1986 £18.00

☐ **Review Article: The Radiological Effects of Nuclear War** (*BJR,* 1983, *56,* 147–170) 50p
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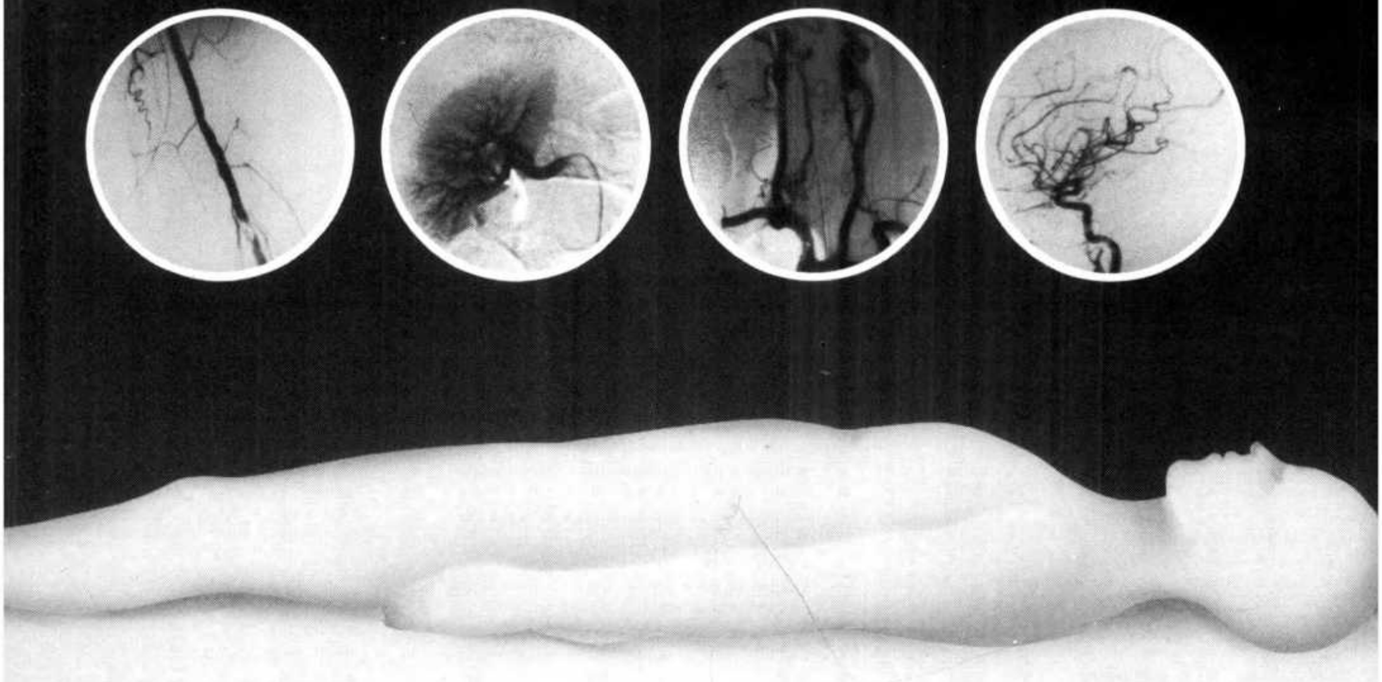

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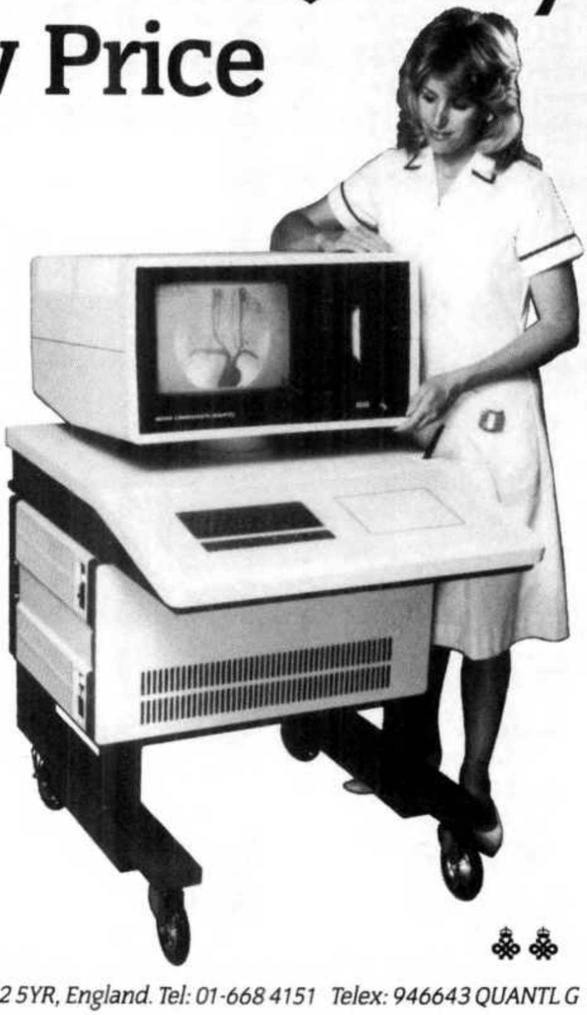

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Volume 59 Number 706
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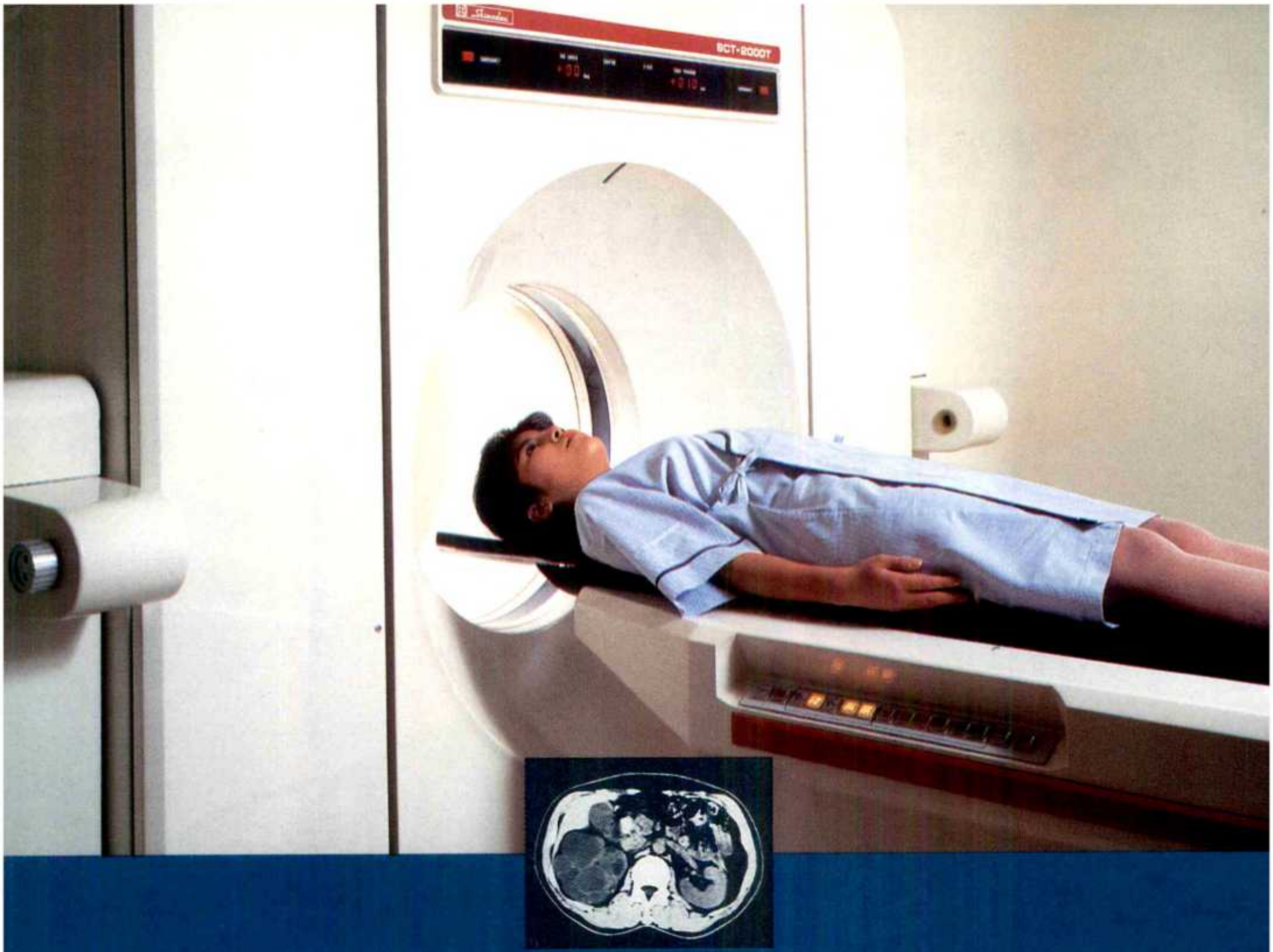

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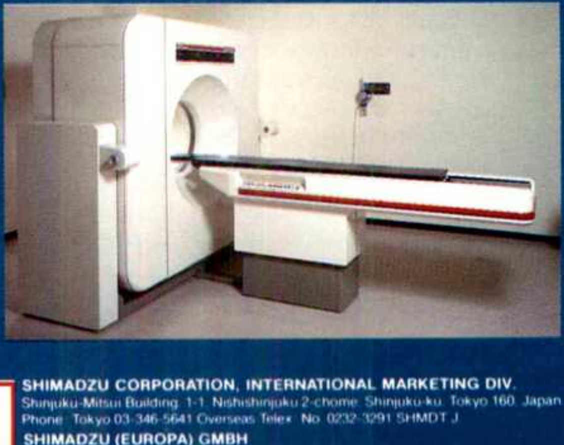

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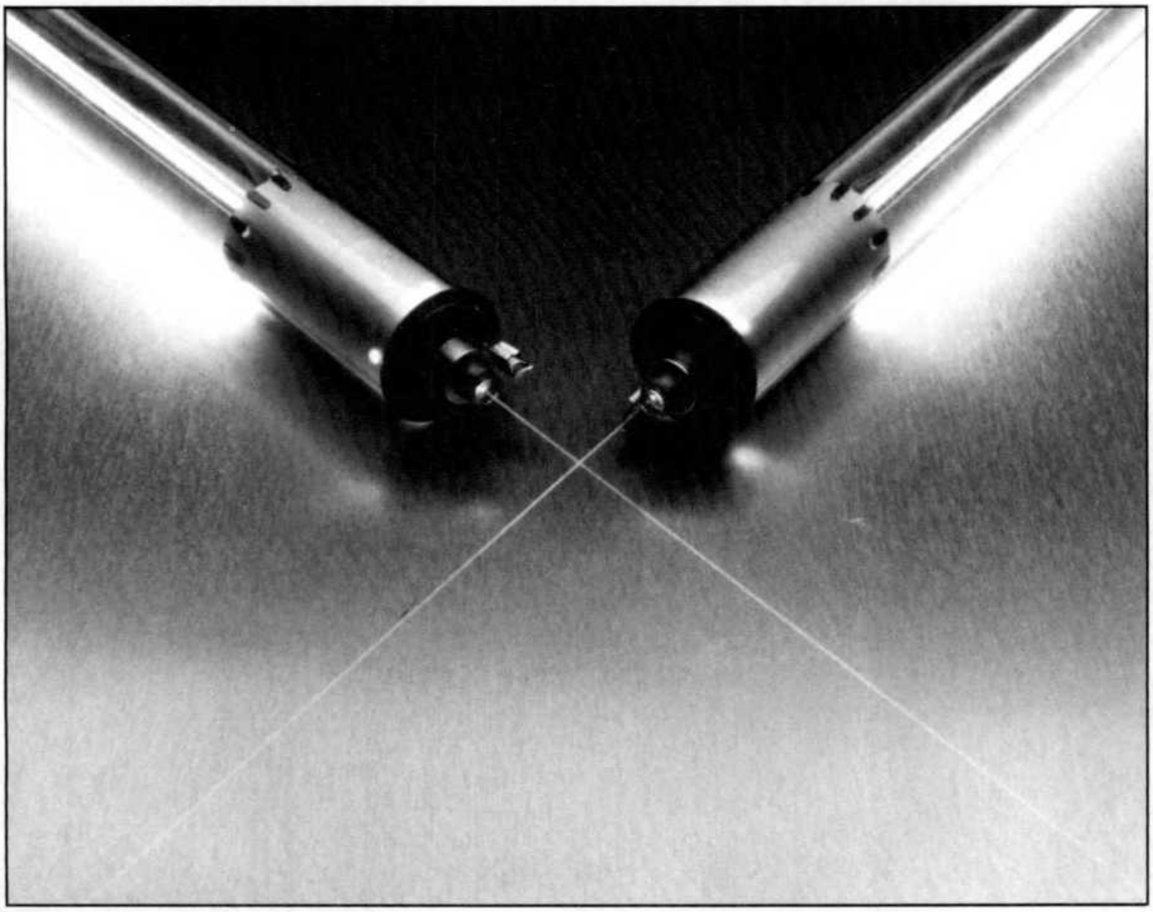

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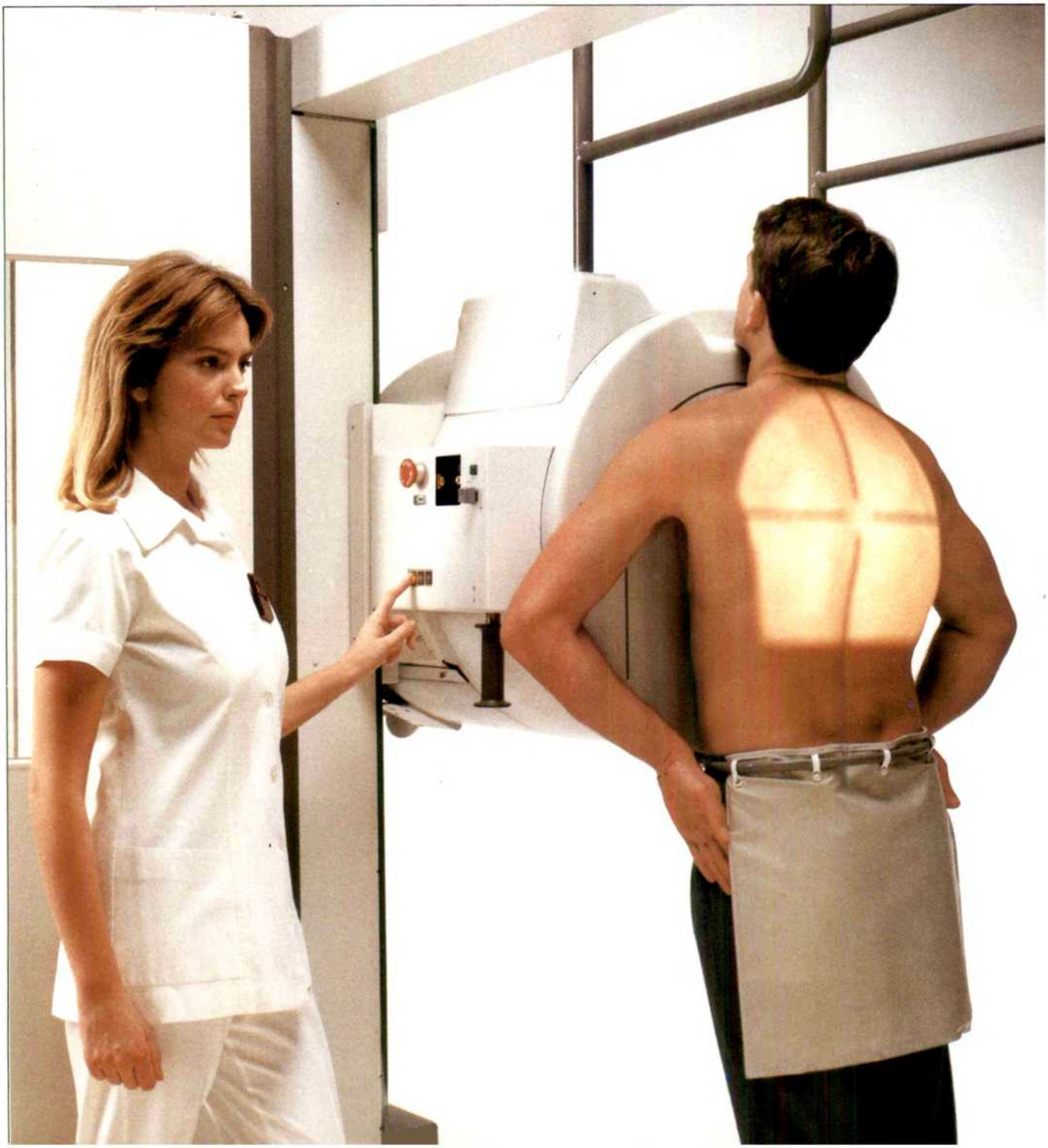

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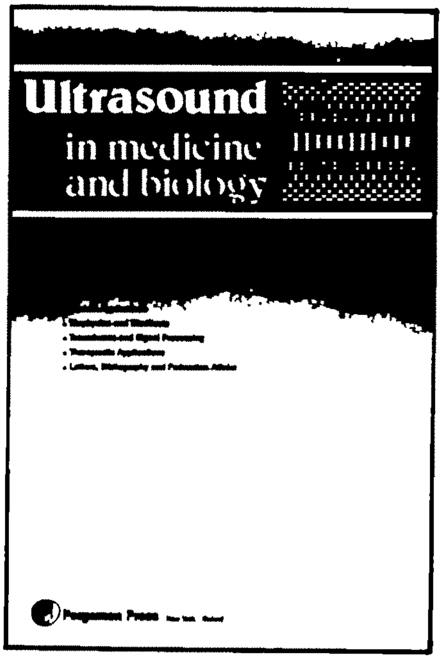

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Official Journal of the World Federation for Ultrasound in Medicine and Biology

Editor: D N WHITE, *230 Alwington Place, Kingston, Ontario K7L 4P8, Canada*

Ultrasound in Medicine & Biology publishes original articles which deal with the interaction of ultrasonic energy with living systems. A major aim of the journal is the promotion of new knowledge concerning the understanding and employment of this form of energy in medicine and biology. The majority of the published papers deal with ultrasonic applications in clinical medicine. Occasionally, review articles or articles of historical interest are featured. There is also a section devoted to Letters to the Editor, where original observations or comments or criticism on the material published in the journal can be printed with a minimum of delay. Reports of scientific meetings and a calendar of forthcoming scientific meetings within the field of interest of the journal are also included.

New Patents Section — The journal now contains abstracts and illustrations of recently issued United States Patents and published patent applications filed from over 30 countries under the Patent Co-operation Treaty.
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Subscription Information

Published monthly (Volume 12)	
Annual subscription (1986)	**US$225.00**
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A selection of papers

Review paper. Contrast echocardiography, J ROELANDT.
Echocardiographic contrast patterns of the right-side of the heart: clinical significance, G GULLACE.
Contrast *M*-mode echocardiography in patients with interatrial communications, G KRONIK.
Videodensitometric processing of contrast two-dimensional echocardiographic data, R S MELTZER *et al.*
Comparison of methods of recording and analysis of Doppler blood velocity signals in normal subjects, S P CREEKMORE *et al.*
Method for estimating the Doppler mean velocity waveform, M S KASSAM *et al.*
A comparison of two calibration methods for ultrasonic hydrophones, W B GLOERSEN *et al.*
The concept of three dimensional resolution in echocardiographic imaging, L JOYNT & R L POPP.
Ultrasonic characterization of acute renal failure, V N GUPTA *et al.*
Measurement of soft tissue motion using correlation between A-scans, R J DICKINSON & C R HILL.
Oil-in-gelatin dispersions for use as ultrasonically tissue-mimicking materials, E L MADSEN *et al.*

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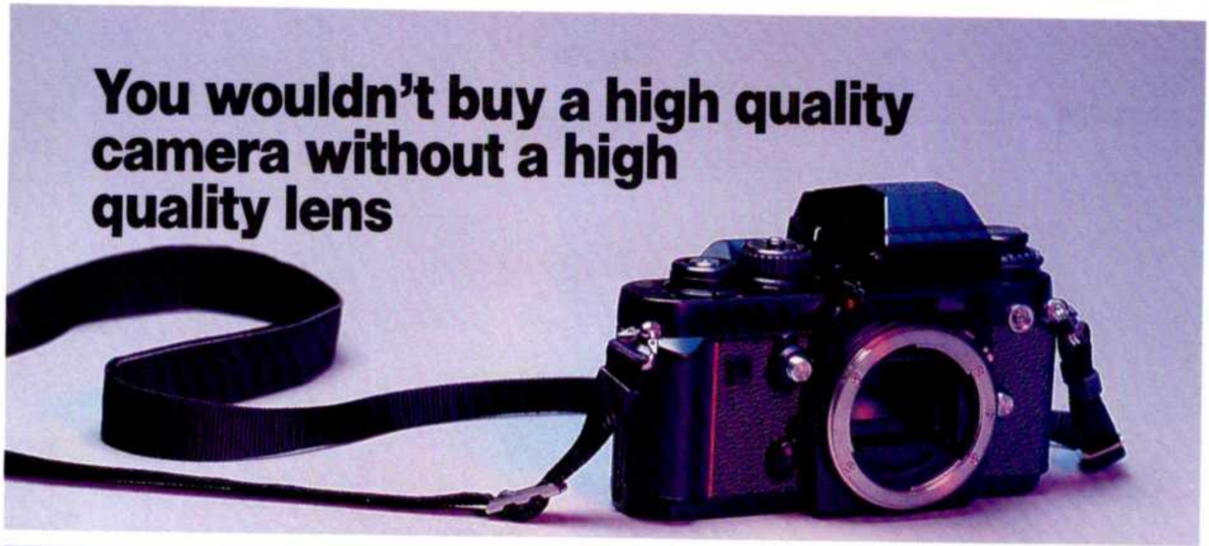
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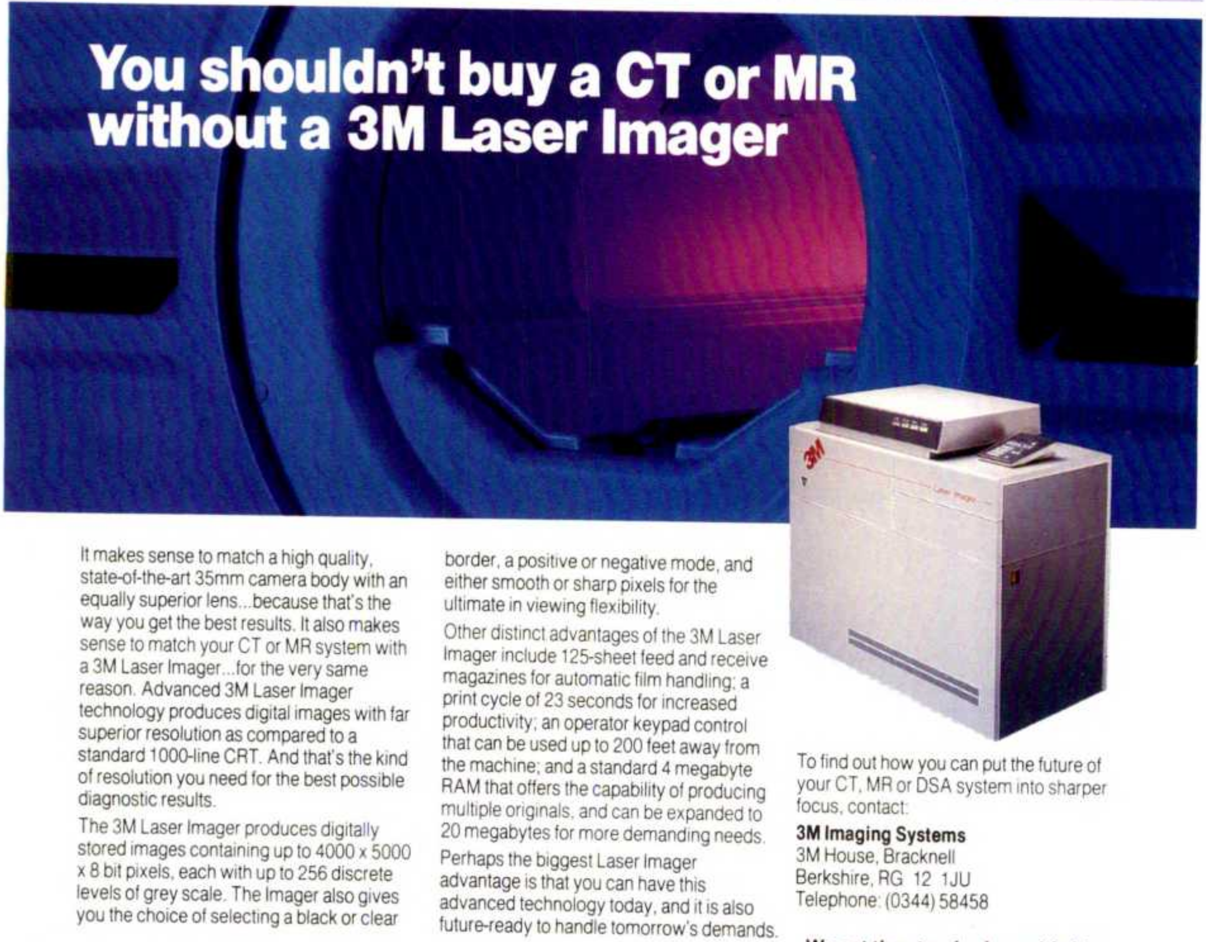

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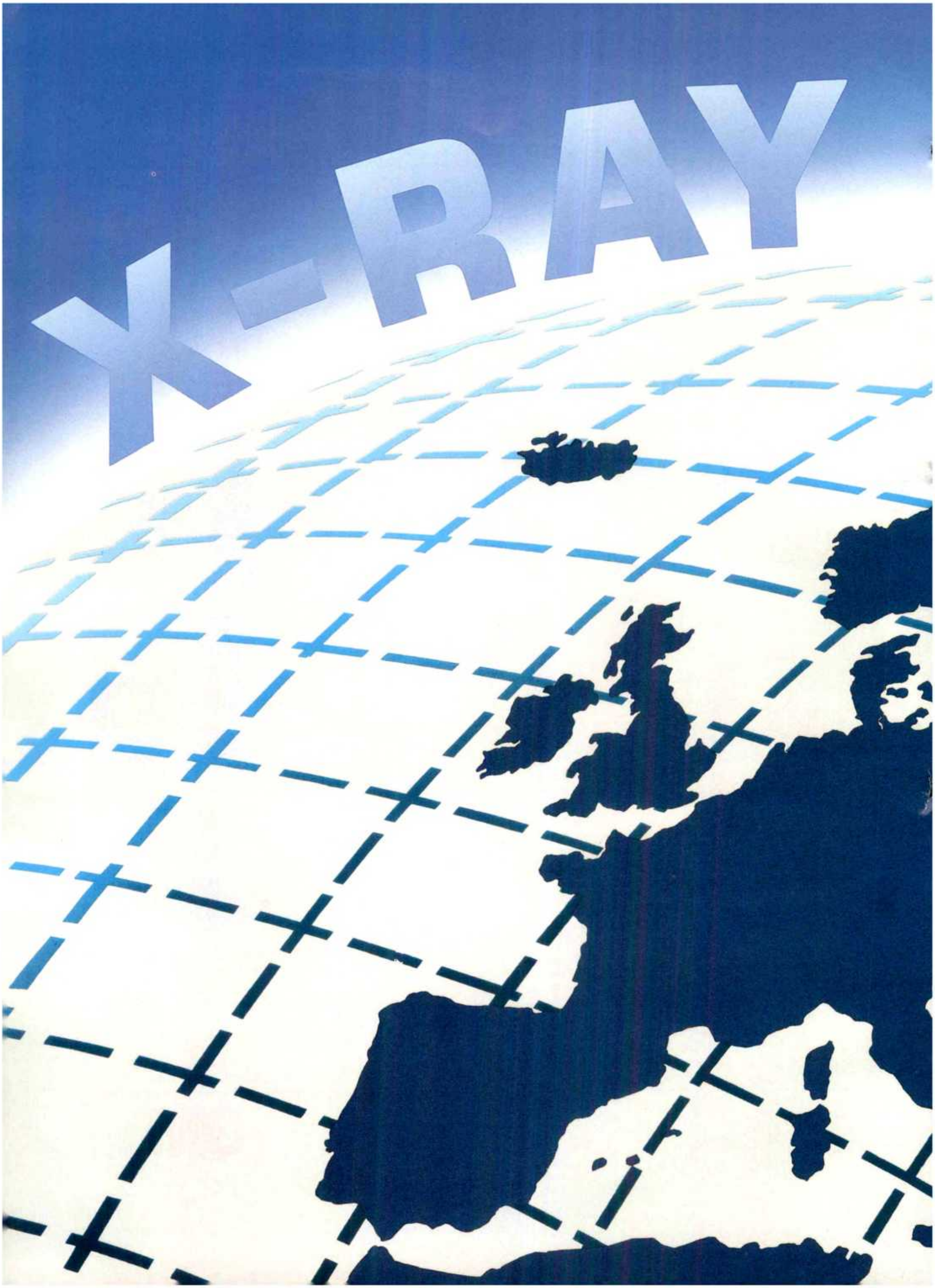
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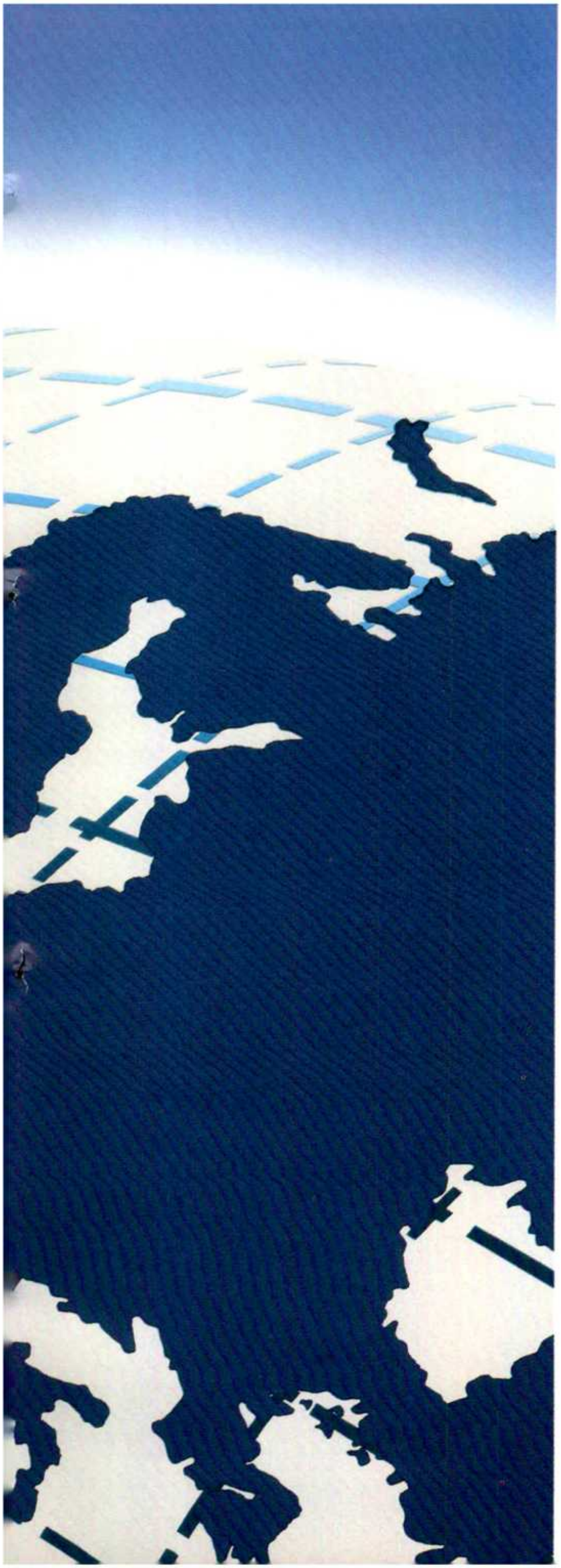

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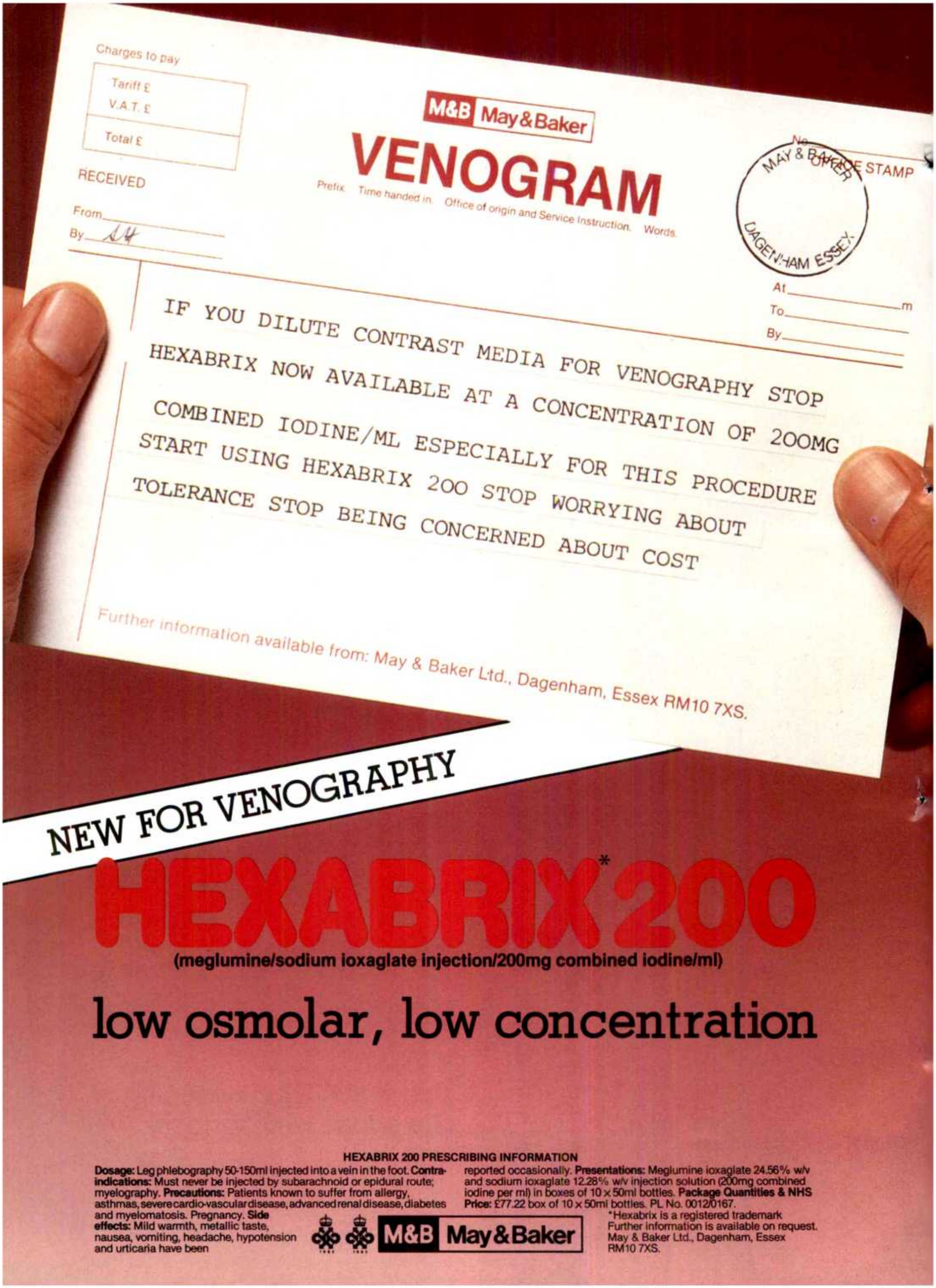

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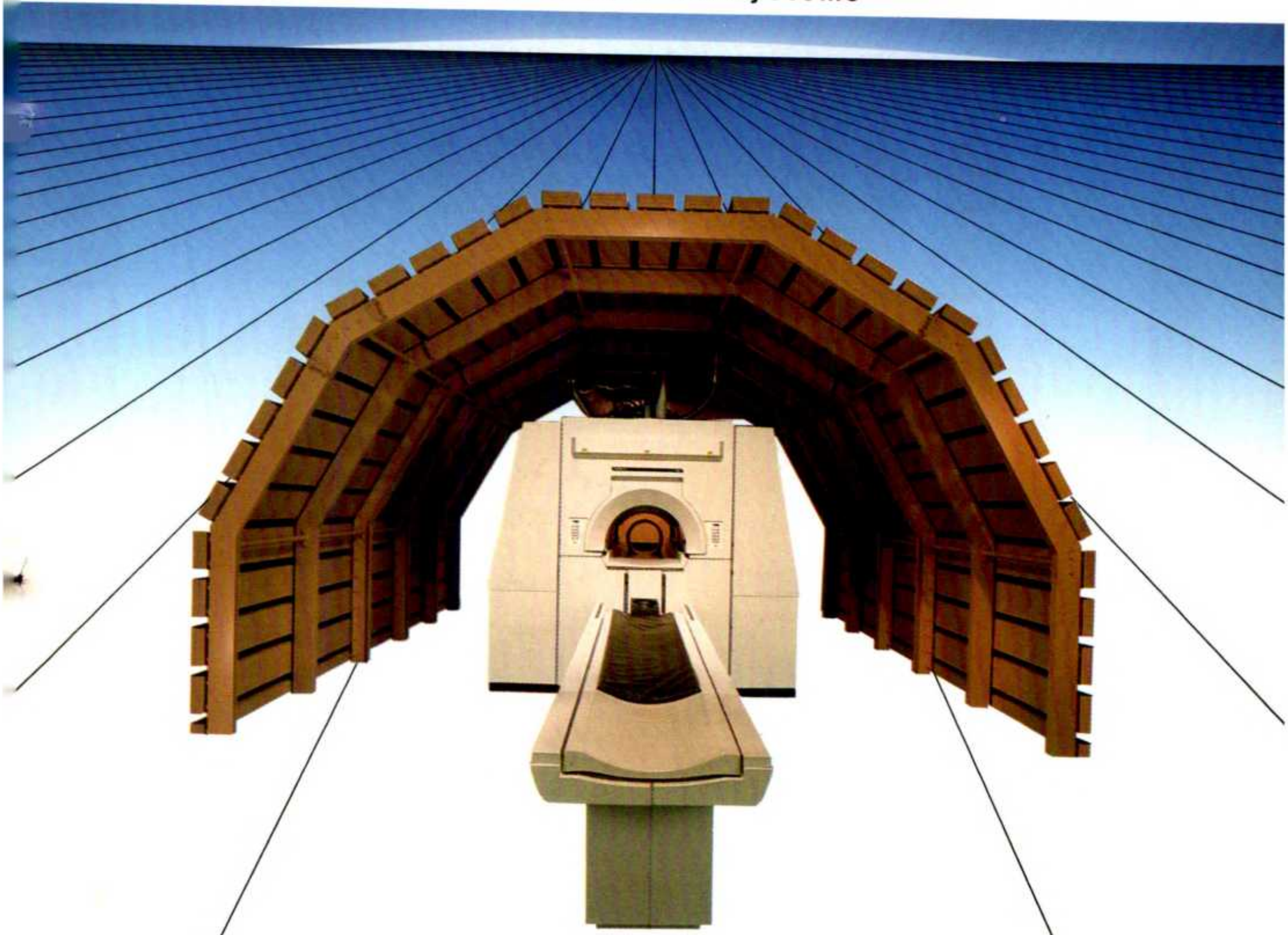

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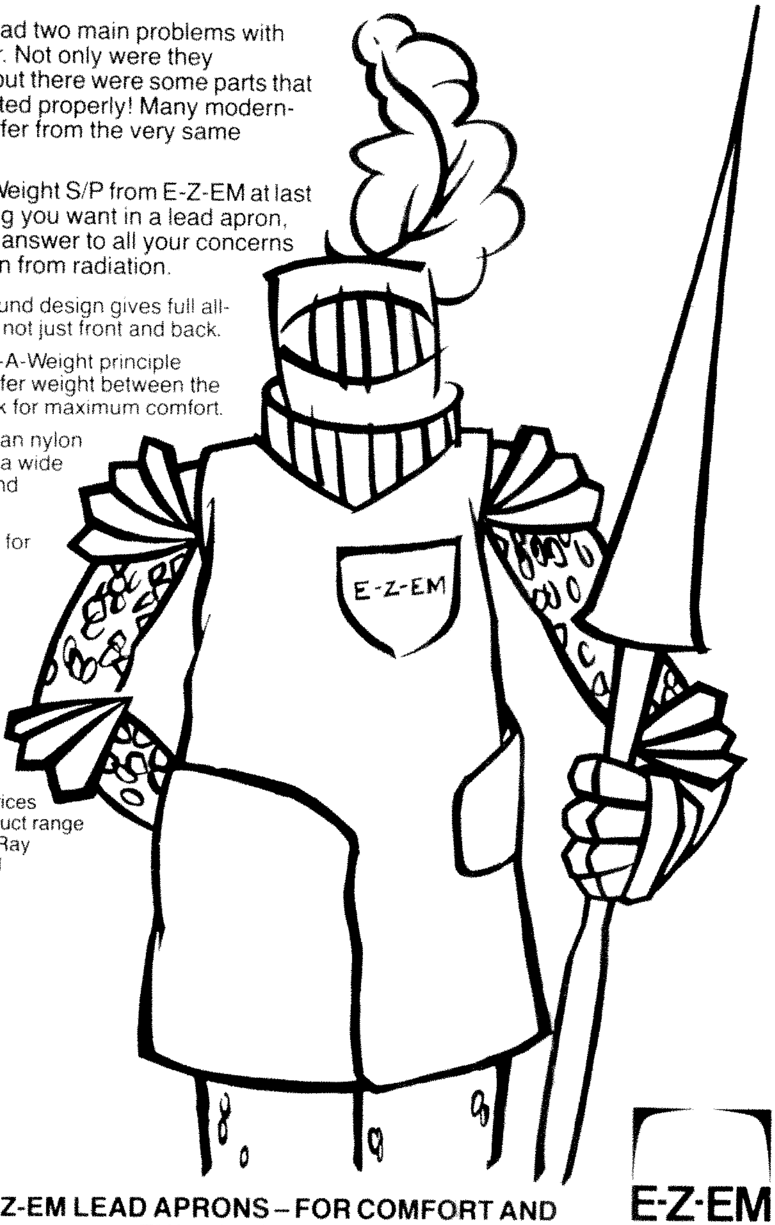

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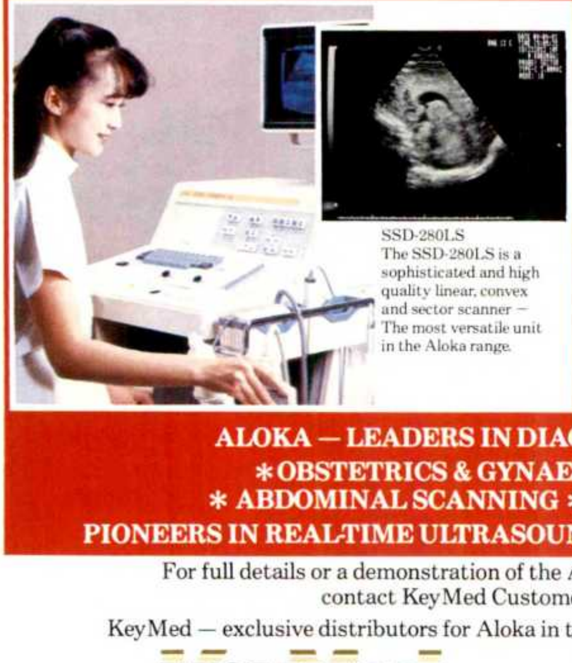

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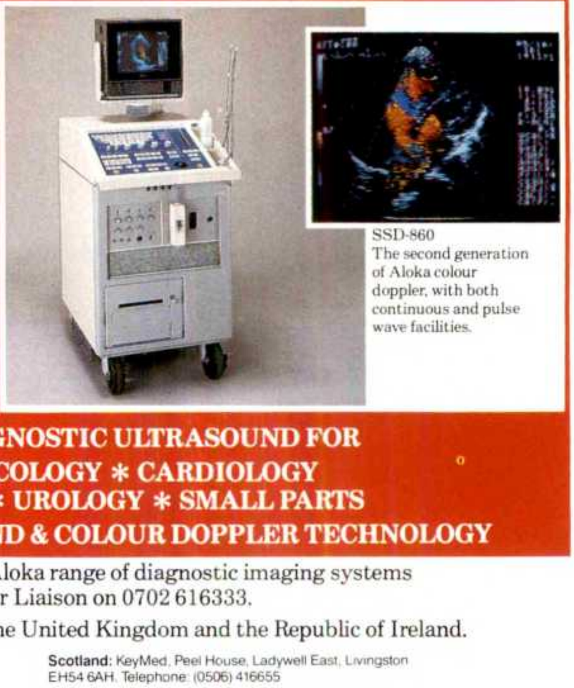

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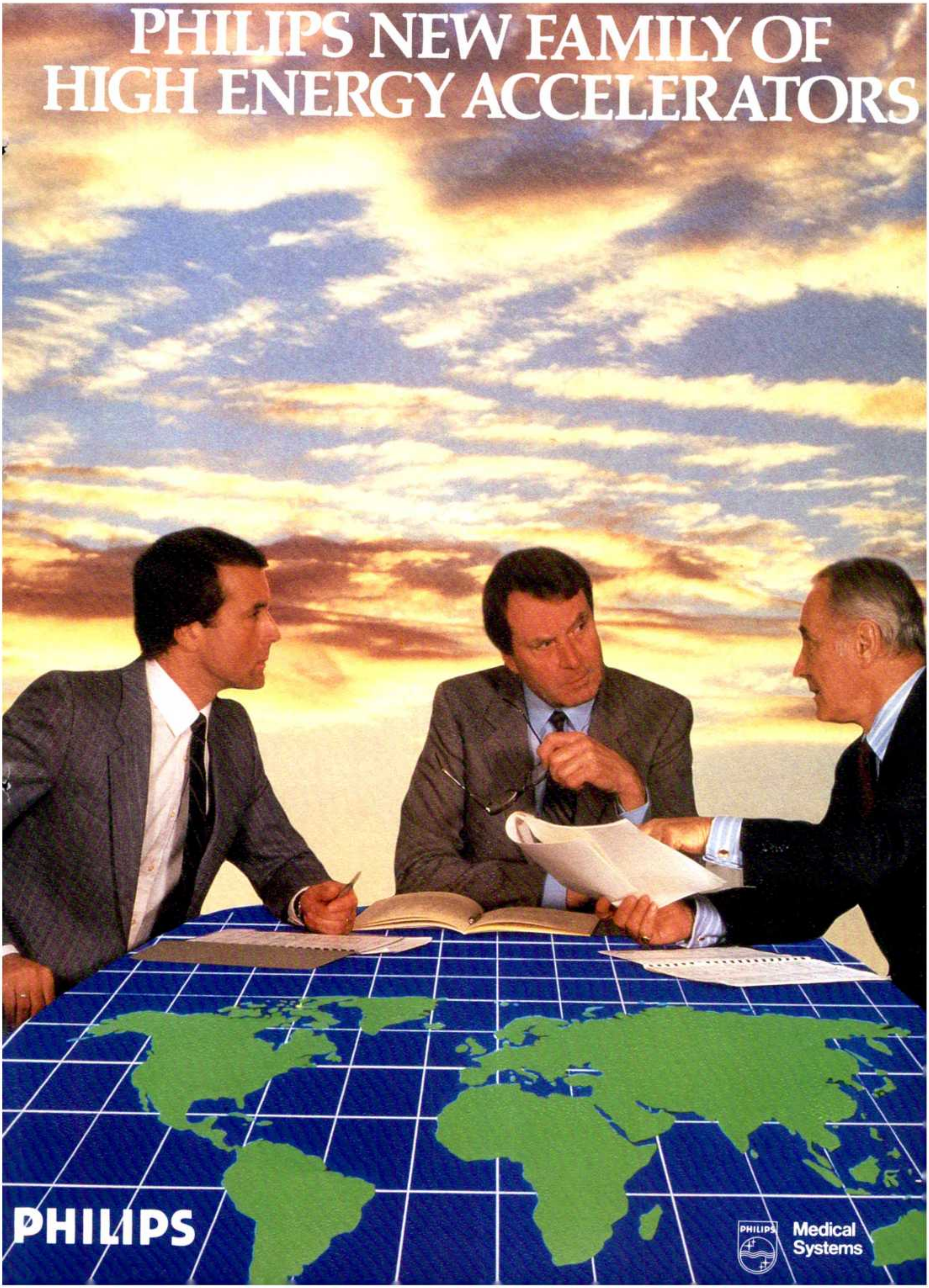
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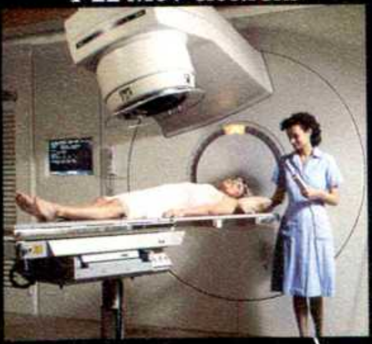

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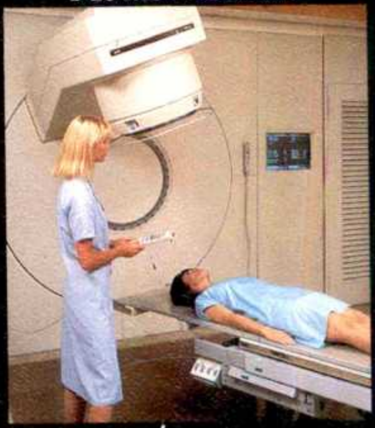

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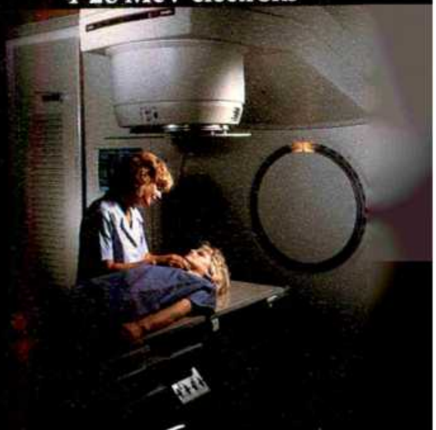

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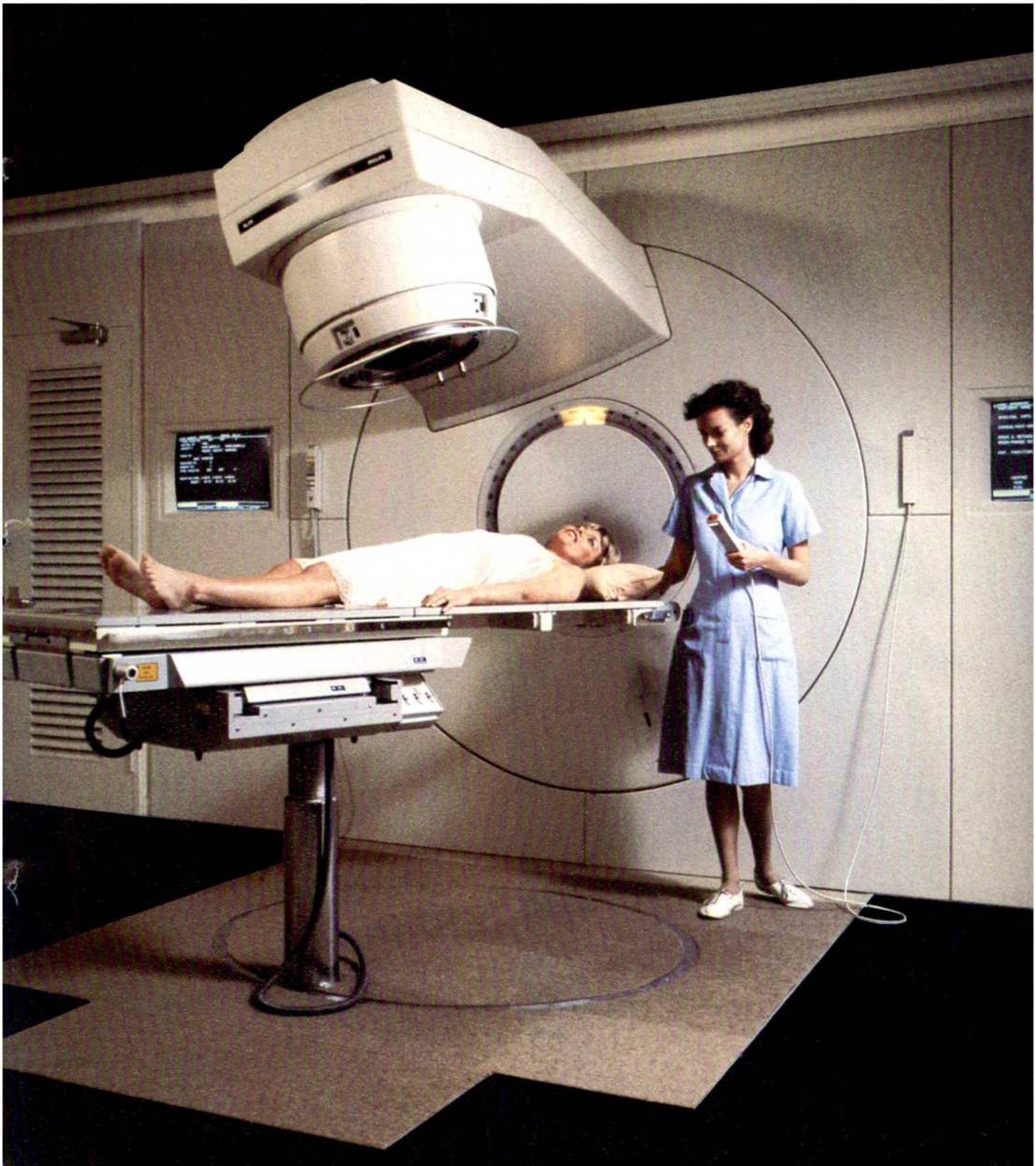

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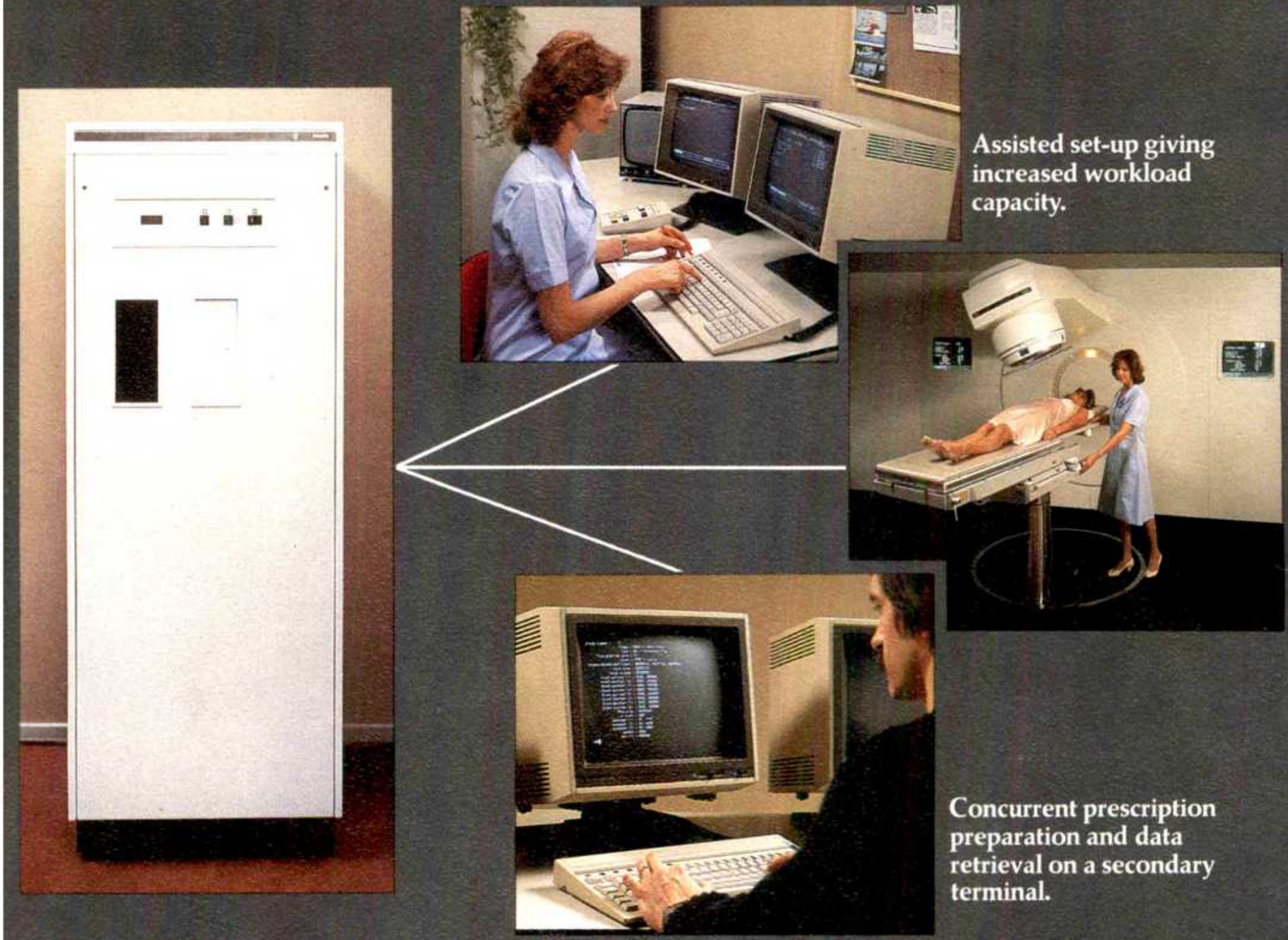

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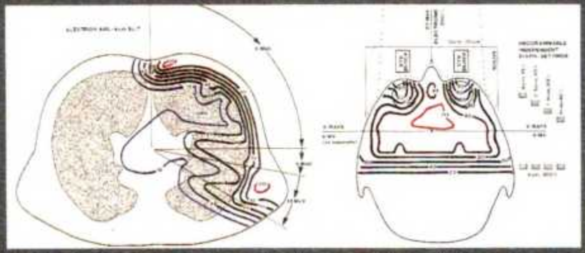

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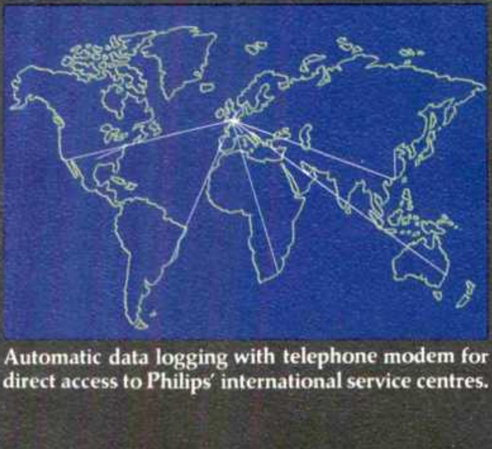

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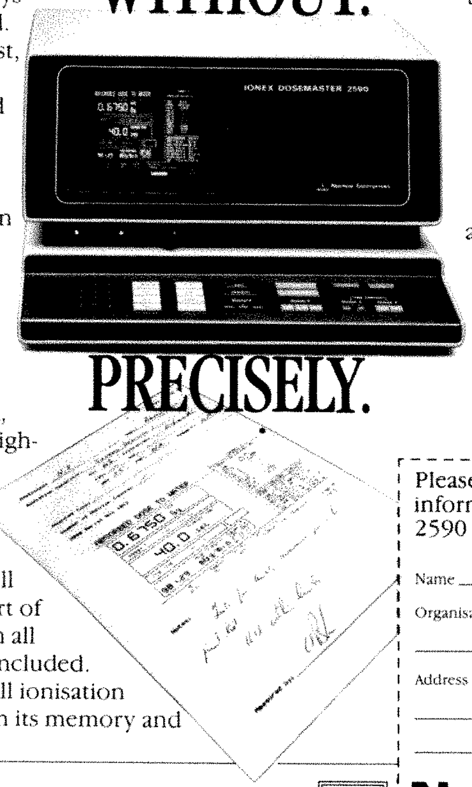

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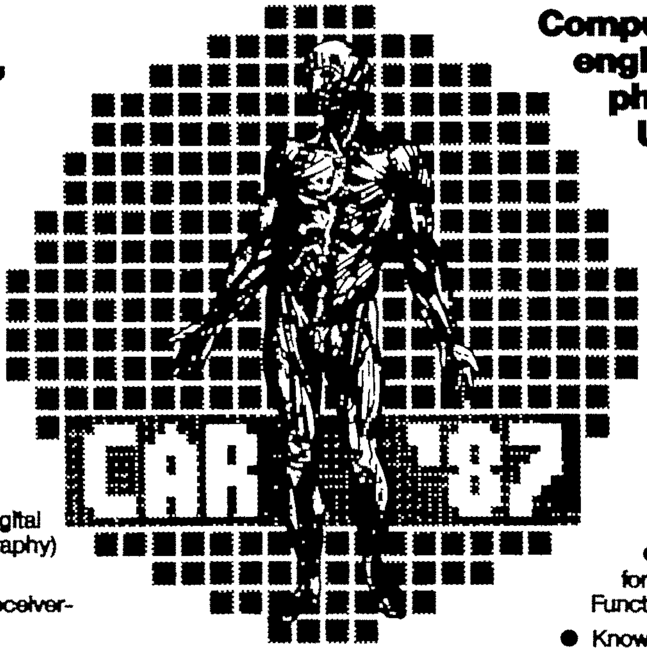

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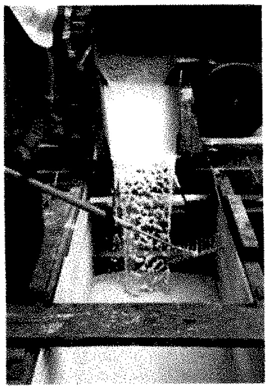

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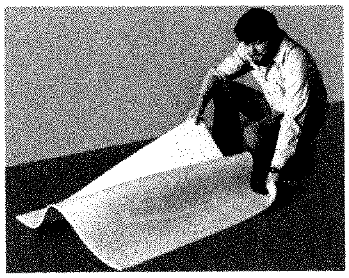

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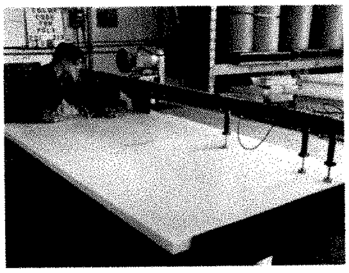

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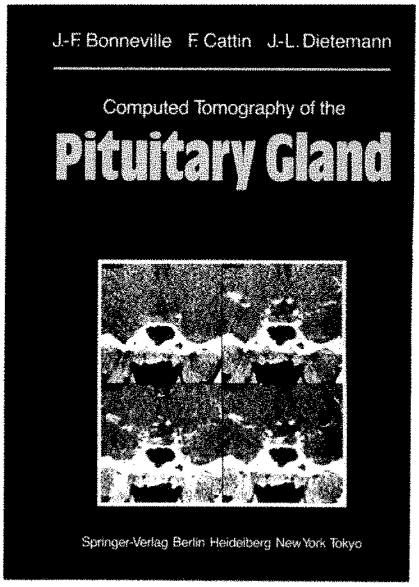

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The British Journal of Radiology

Magnetic resonance imaging of the cerebello-pontine angle

By R. R. Mawhinney, M.B., Ch.B., F.R.C.R., J. H. Buckley, M.B., B.Ch., M.R.C.P., F.R.C.R. and B. S. Worthington, B.Sc., M.B., B.S., F.R.C.R.

Academic Department of Radiology, Queen's Medical Centre, Nottingham

(*Received March 1986*)

ABSTRACT

A variety of extra-axial lesions occurring at the cerebello-pontine angle was examined by magnetic resonance imaging (MRI). Differences in spin sequence characteristics were found between neurilemmomas and meningiomas, with neurilemmomas exhibiting a greater increase in T_2 than meningiomas. The T_1 images were of less value in differentiating between neurilemmomas and meningiomas but were of value in the diagnosis of vascular lesions, due to the decreased T_1 of blood clot. The T_1 images were also of value in the assessment of tumour size and in the diagnosis of an epidermoid cyst. Extension of tumour into the internal auditory meatus was seen on MRI with acoustic neuromas and with one other lesion. The transverse perspective was of greatest value in lesion assessment. The coronal perspective was useful in certain situations but the sagittal perspective was of minimal clinical value.

Magnetic resonance imaging (MRI) was recognised early to be an excellent imaging technique for posterior fossa lesions (Bydder et al, 1983) and the cerebello-pontine angle (CPA) has received considerable attention with respect to the commonest tumour found at this site, namely acoustic neuromas (Young et al, 1983; DeFilipp & Buchheit, 1985; Kingsley et al, 1985). Magnetic resonance imaging is of particular value since even small lesions, previously visible only by computed tomography (CT)-assisted air meatography, can be imaged directly (Young et al, 1983; New et al, 1985). Sensitivity can be further improved by the use of gadolinium-DTPA (Curati et al, 1985).

Other lesions, notably meningiomas and epidermoids, though considerably less common than acoustic neuromas (Hitselberger & Gardener, 1968; Kieffer et al, 1975; Olson et al, 1978) do, however, occur at the CPA and may present diagnostic difficulties on CT (Claveria et al, 1977; Rao & Woodlief, 1979).

The MRI characteristics of a variety of lesions occurring at the CPA were examined. Particular reference is made to features of use in differential diagnosis and to areas where MRI may have an advantage over other imaging techniques, especially CT. As mentioned above, because acoustic neuromas constitute some 80% of CPA lesions and meningiomas about another 10%, all other lesions are relatively rare. In these latter cases, observations are, of necessity, preliminary. Where numbers are larger, an attempt has been made to analyse specific features.

PATIENTS AND METHODS

Twenty-three patients with extrinsic lesions involving the CPA are included: details are given in Table I. All cases were confirmed either by surgery or by post-mortem examination and subsequent histology, with the single exception of an epidermoid, where diagnosis was based on typical CT features (Fig. 9E). Purely intracanalicular neuromas and other cases without histological confirmation are excluded.

The majority of patients had either a neurilemmoma or a meningioma (mean patient ages of 42.5 and 46 years, respectively). Two neurilemmomas did not arise from the VIII nerve. One arose from the IX nerve. The origin of the other was obscure but it was not from VII, VIII or IX nerve.

Magnetic resonance scans were performed on a commercial Picker 0.15 T resistive system using a multislice technique with non-contiguous cuts 10 mm thick. A variety of spin sequences and scan planes were employed. The mean number of sequences was 3 (range 2–5) and the mean number of scan planes was 2.3 (range 1–3) per patient. Spin sequences included an inversion-recovery (IR) sequence in all but one patient (who could not tolerate the scanner long enough) and all but one (a 5-year-old girl for the same reason) had an essentially T_2-weighted spin-echo (SE) sequence.

All patients also had a CT scan, most being performed on a fourth-generation scanner with a high resolution mode.

All lesions were assessed with respect to their spin characteristics on T_1- and T_2-weighted images. A comparative seven-point scale of signal intensity was employed, using normal tissues as reference, for both T_2 images (SE: $TE > 60$; $TR > 1000$) and T_1 images (IR: $TI = 500–600$; $TR = 1500–2000$). Details are given in Table II. The petrous bone allowed a clear separation between scores -2 and -3. Separation between $+2$ and $+3$ was more subjective. A lesion was scored $+3$ when its signal appeared greater than all other surrounding structures, including subcutaneous fat. The scoring system is illustrated by Figs 1A, 1D, 2, 4B and

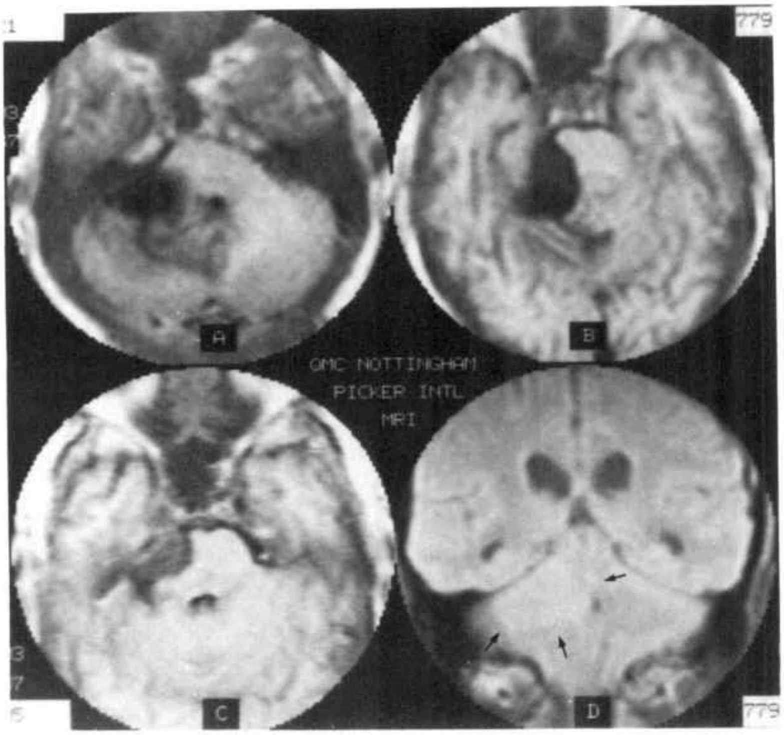

FIG. 1.

Meningioma. (A) IR 1800/500. The meningioma is seen as a very low-signal lesion occupying the right CPA. Tumour signal is lower than the adjacent petrous bone (score, IR −3). (W = 903, L = 247.) (B) IR 1800/500. Scan at a slightly higher level than (A) showing extension above the petrous ridge. (W = 903, L = 247.) (C) IR 2000/600. Repeat scan 1 year later, after surgery, showing recurrence of the meningioma. Even allowing for the slightly different sequence, the lesion shows an undoubted increase in signal intensity from the original scan. (W = 903, L = 247.) (D) Coronal SE 1000/60. The meningioma (arrows) shows the same signal intensity as grey matter, making identification difficult (score, SE + 1). (W = 799, L = 364.)

6A. Tumour homogeneity, the presence or absence of a low-signal rim surrounding the lesion and extension into the internal auditory canal (IAC) were noted.

RESULTS

Lesion spin sequence characteristics are detailed in Table III. It can be seen that neurilemmomas generally have more extreme scores than meningiomas. No meningioma scored +3, whereas 50% of neurilemmomas did so, and the combined SE and IR score (SE + IR) did not exceed four, while 60% of the neurilemmoma group scored five or six. A very long T_1 was also found with four neurilemmomas. One meningioma and one epidermoid had a similarly prolonged T_1.

TABLE I

CEREBELLO-PONTINE ANGLE LESIONS BY PATHOLOGY

	No. of patients
Neurilemmoma (VIII nerve)	8
Neurilemmoma (other)	2
Neurofibroma (bilateral)	1 (2 lesions)
Meningioma	5
Epidermoid	2
Rhabdomyosarcoma	1
Cavernous haemangioma	1
Chronic abscess	1
Aneurysm	2
Total	23 (24 lesions)

Of the 19 tumours imaged by both T_2-weighted SE and by IR sequences, the tumours were seen better on T_2 images in 11, equally well in six, and better on IR in two. The limitation of the IR sequence at the CPA is largely due to difficulty in separating tumour from the petrous bone, which often has the same signal (Fig. 4B). While T_2 sequences are, therefore, generally superior, they may, nevertheless, be misleading. In two cases, T_1 images were more accurate in assessing tumour extent (Fig. 4). The IR sequences also provided convincing evidence of the presence of blood clot in the case of the aneurysms. This was sometimes confirmed by the finding of flow-related enhancement and more specifically led to sequences to demonstrate the abnormal blood-flow using even-echo rephasing techniques (Bradley & Waluch, 1985) (Fig. 5).

Of the eight acoustic neuromas, there was widening of the internal auditory meatus (IAM) as assessed by

TABLE II

COMPARATIVE SCORING OF LESION SIGNAL INTENSITY

Signal intensity of lesion (L)	Score
$L \gg$ grey matter	+3
$L >$ grey matter	+2
$L =$ grey matter	+1
$L =$ brain stem	0
Petrous $< L <$ brain stem	−1
$L =$ petrous bone	−2
$L <$ petrous bone	−3

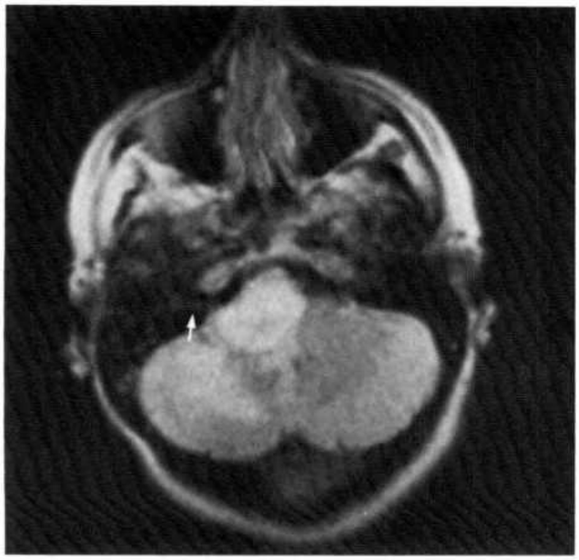

FIG. 2.

SE 1000/60. Petrous meningioma extending into the CPA. The lesion shows a higher signal than grey matter (score, SE+2). The right IAC (arrow) is normal. (W = 914, L = 435.)

CT in six cases. Widening was also produced by a cavernous haemangioma (Fig. 7) but by no other lesion. Of these seven cases with IAC widening on CT, extension into the IAM was visible in five on MRI (Figs 3A, 4A and 7A).

The presence of a low-signal rim, suggesting an extra-axial lesion (Zimmerman et al, 1985), was found in three cases (Figs 1B, C and 6). Two of these were neurilemmomas and the other was a meningioma.

Tumour homogeneity was also assessed. Both the meningioma and the neurilemmoma group showed evidence of tumour heterogeneity in roughly half the cases. While heterogeneity was often better demonstrated on either the T_1 or T_2 sequence in individual cases, overall neither sequence was more sensitive than the other.

Both epidermoids were consistent in showing a high signal on T_2-weighted sequences but showed differing appearances on IR. One had an increased signal on T_1 images (Fig. 8D) while, conversely, the other demonstrated a very low signal, indicating a prolonged T_1 (Fig. 9B, C).

The transverse plane was undoubtedly the most satisfactory for imaging the CPA, giving the best demonstration of mass effect and extension, where present, of tumour into the IAC. The coronal perspective was of some value with large lesions in demonstrating anatomical relationships, particularly to the tentorium (Figs 1D and 9D), and was the only projection which clearly demonstrated the extra-axial component of a chronic abscess (Fig. 10D). In no case was the sagittal perspective of any specific diagnostic or clinical value.

DISCUSSION

Our results suggest that the finding of a high-signal-intensity lesion at the CPA on T_2-weighted sequences is against the diagnosis of a meningioma. This is at variance with a recent report which found signal intensity to be of no value in differentiating meningiomas from neurilemmomas (Mikhael et al, 1985). That report, however, looked at only two meningiomas and is not supported by other workers, who have shown meningiomas to be unusual in comparison with other tumours in having relatively short T_1 and T_2 times (Bydder & Young, 1985). This results in meningiomas exhibiting only minimal increase in intensity with increasing T_2 weighting (Bradley et al, 1985). The use of even more strongly T_2-weighted sequences could therefore have been expected to produce an even greater separation of meningiomas from other tumours than our results suggest.

Forty per cent of the neurilemmoma group had a

TABLE III

SPIN INTENSITY SCORES AGAINST PATHOLOGY

Pathology	No. of cases					
	Spin-echo (T_2) score			Inversion-recovery (T_1) score		
	+3	+2	+1	−1	−2	−3
Neurilemmoma	5	4	1	1	4	4
Meningioma	0	2	3	1	3	1
Neurofibroma	0	0	2	0	2	0
Epidermoid	2	0	0	0	1 (+2)	1
Cavernous haemangioma	1	0	0	0	0	1 (+3)
Aneurysm	1	1	0	0	1 (+2)	1 (+3)
Chronic abscess	1	0	0	1	0	0

Numbers in brackets represent positive values on IR. The rhabdomyosarcoma is not included as no T_2 sequence was performed. One neurilemmoma had no IR sequence.

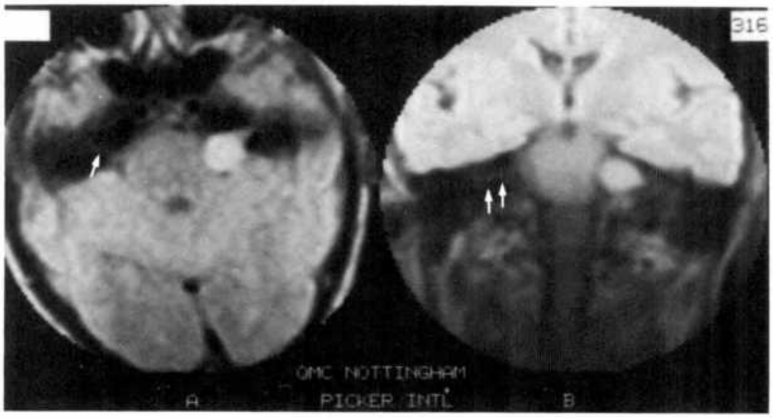

FIG. 3.

Acoustic neuroma. (A) SE 1200/80. Classical appearances of an acoustic neuroma showing extension into the IAC. Normal right IAC (arrow). (W = 639, L = 367.) (B) Coronal SE 1200/40. The normal right IAC is seen (arrows) while on the left, tumour is seen directed into the canal. Note also decreased tumour signal intensity on this less T_2-weighted sequence. (W = 1195, L = 460.)

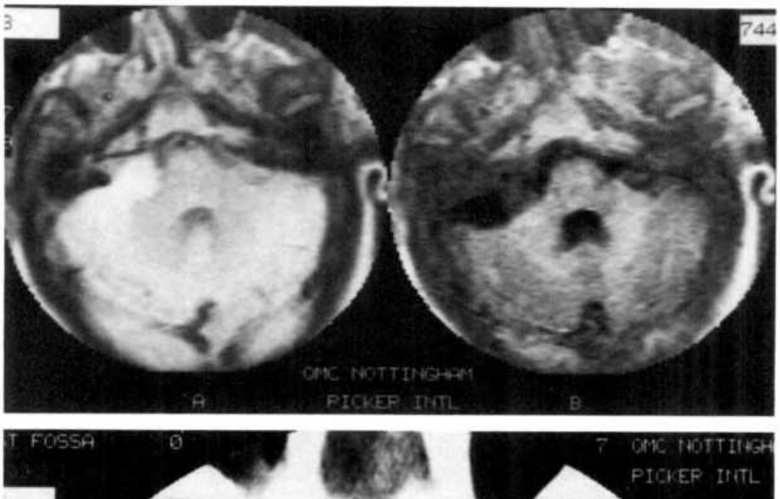

FIG. 4.

Acoustic neuroma. (A) SE 1500/60. Widening of the IAC is again apparent. The borders of the tumour are not defined laterally. (W = 527, L = 209.) (B) IR 2000/500. The tumour cannot be differentiated from petrous bone (score, IR −2) but its boundaries within the CPA are more accurately defined due to contrast with adjacent cerebrospinal fluid. (W = 864, L = 237.) (C) Enhanced CT scan (W = 157, L = 58). Close correlation with the IR image is seen.

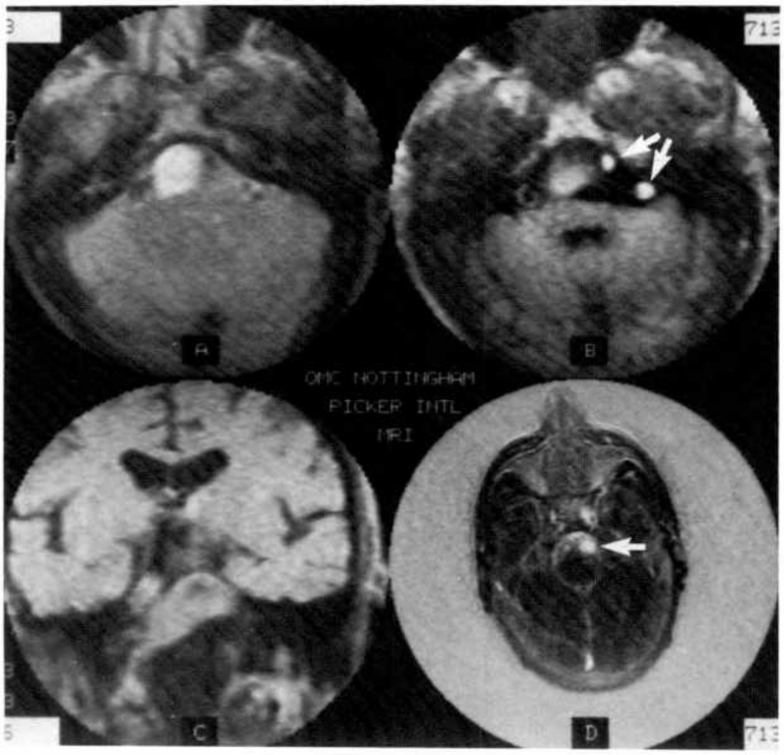

FIG. 5.

Basilar artery aneurysm. (A) SE 2000/80. An area of high signal is present anterior and slightly to the right of the pons. (W = 913, L = 337.) (B) IR 1800/400. At the same level as (A). High signal is seen at the same site, indicating either blood clot or fat. Very high signal (arrows) is present due to paradoxical enhancement from slow-flowing blood. (W = 1038, L = 364.) (C) Coronal SE 500/40. The aneurysmal basilar is seen running obliquely anterior to the brain stem. (W = 853, L = 383.) (D) Even echo subtraction (TE 22 and 41: TR 1000). Confirms the presence of flowing blood by demonstrating high signal within the lesion (arrow). (W = 328, L = −25.)

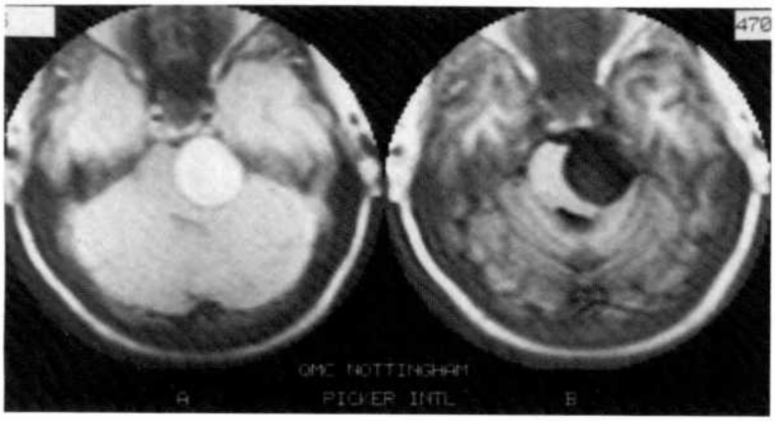

FIG. 6.

Neurilemmoma. Not arising from VIII nerve. (A) SE 1200/80. The lesion shows a high signal on this T_2-weighted sequence (score, SE + 3). Note the surrounding low-signal rim (see text). (W = 949, L = 257.) (B) IR 2000/500. Low tumour signal with the surrounding low-signal rim again well seen. (W = 949, L = 158.)

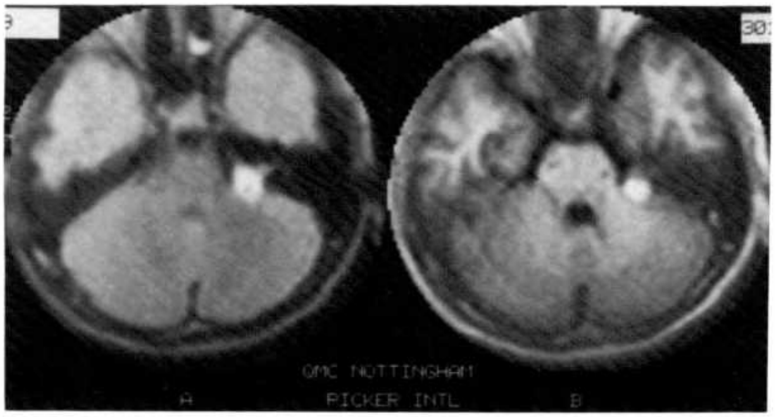

FIG. 7.

Cavernous haemangioma. (A) SE 1200/80. The lesion is clearly seen with extension into the IAC. (W = 982, L = 347.) (B) IR 2000/500. High signal is seen localised at the CPA and the IAC is not seen. The presence of either fat or blood clot is implied. At surgery haemorrhage into the lesion was confirmed. (W = 982, L = 250.)

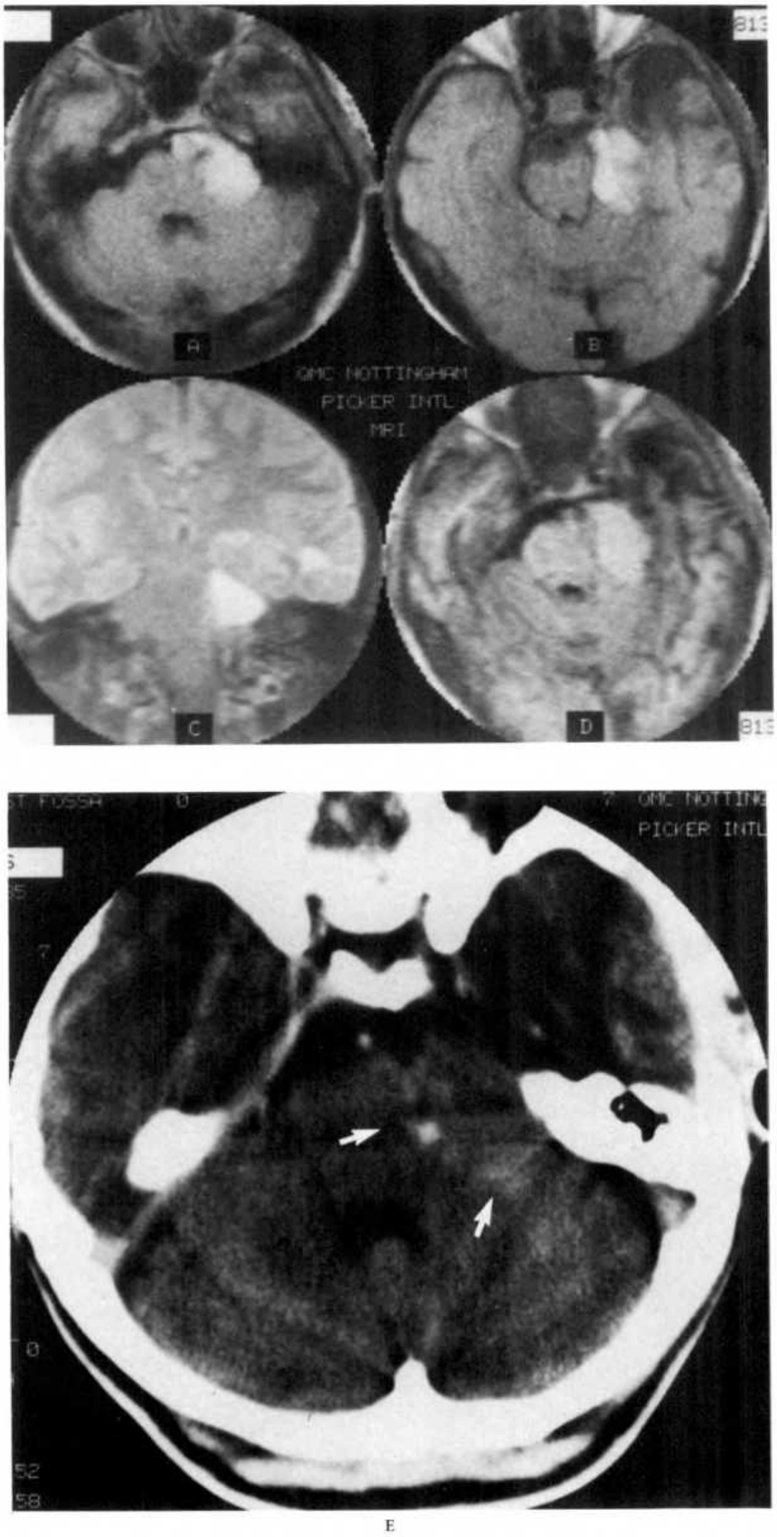

FIG. 8.

Epidermoid. (A) SE 500/40. A lobulated mass lesion is seen within the left CPA. (W = 837, L = 336.) (B) SE 500/40. The tumour extends superiorly distorting the brain stem. (W = 818, L = 334.) (C) Coronal SE 2000/80. The lesion demonstrates very high signal on this T_2-weighted sequence. (W = 1511, L = 428.) (D) IR 2000/500. The lesion shows high signal on this T_1 sequence representing blood or, in this case, fat. (W = 1197, L = 307.) (E) Enhanced CT scan (W = 152, L = 58). Scan at the same level as (A). The lesion (arrowed) is poorly defined, causing difficulty in assessing its full extent.

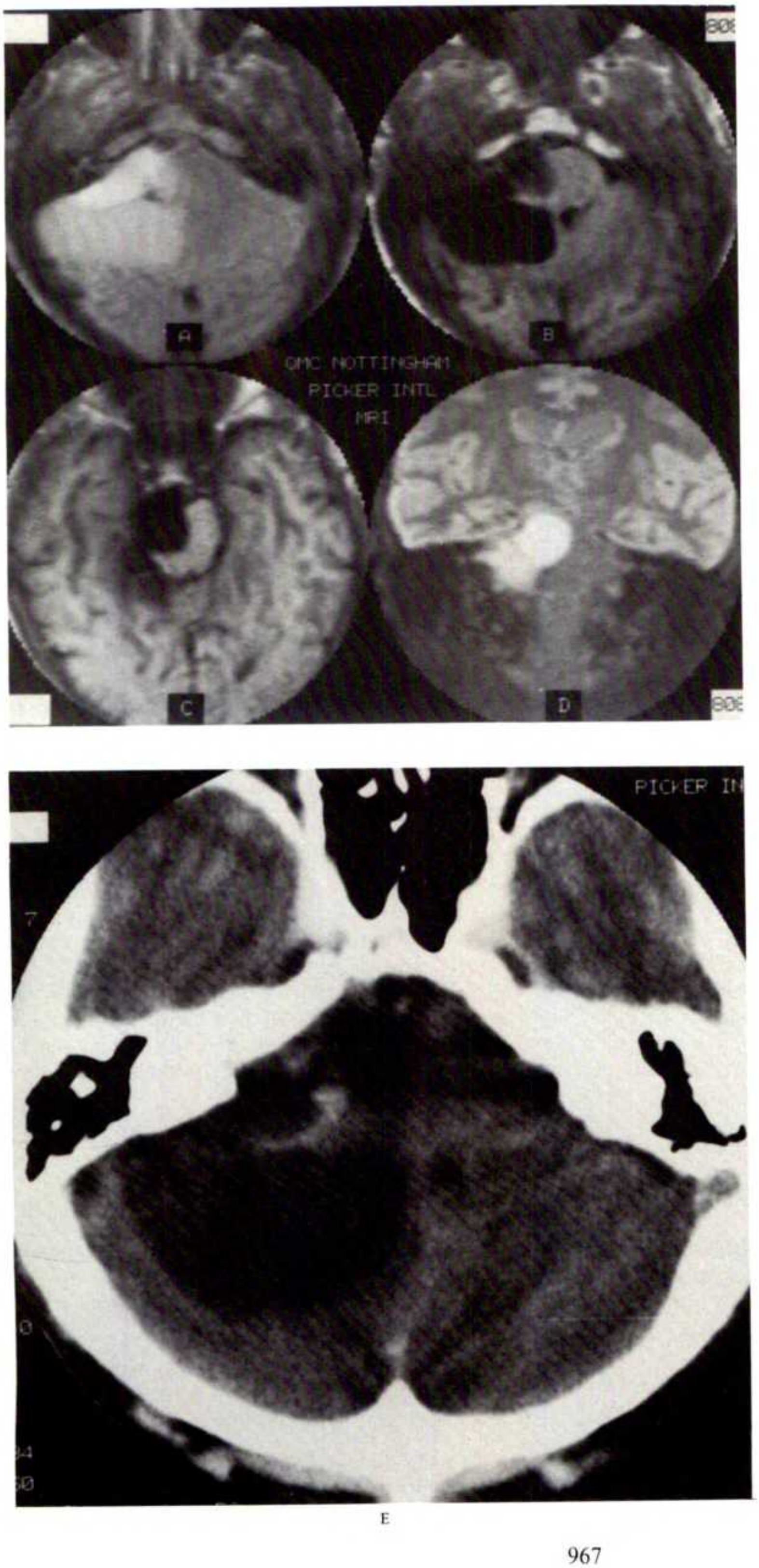

FIG. 9.

Epidermoid. (A) SE 2000/80. A large lobulated mass lesion is present in the right CPA. The IAC is normal. (W = 1141, L = 418.) (B) IR 1800/500. At the same level as (A). The margins of the lesion are better defined due to very low signal contrasted against normal brain. (W = 1126, L = 415.) (C) IR 1800/500. Superior extension with distortion of the brain stem is seen (W = 1126, L = 415.) (D) Coronal IR 1500/100. This short time-inversion (TI) sequence conversely shows the lesion as a high-signal mass. The coronal perspective allows addition appreciation of anatomical relationships. (W = 1269, L = 445.) (E) Enhanced CT scan (W = 184, L = 60). Lobulated low-attenuation mass showing close correlation with the IR sequence (B) though margins are less clearly defined.

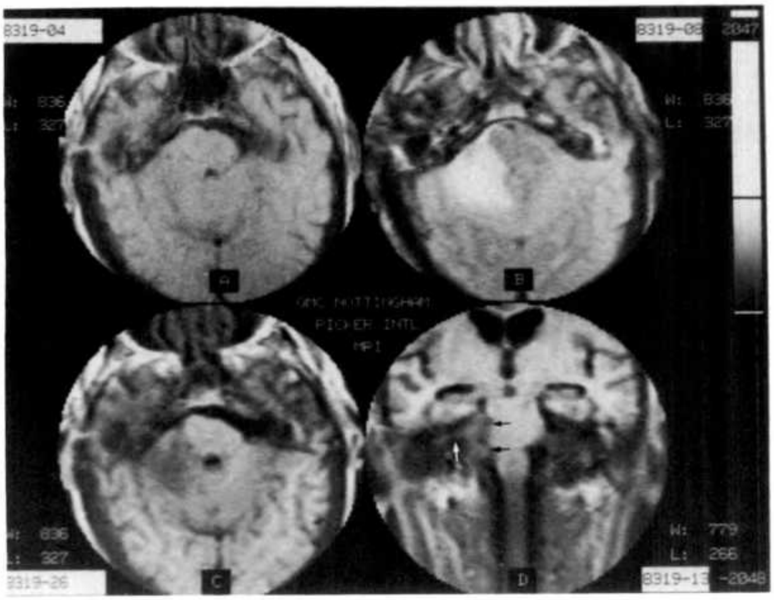

FIG. 10.

Chronic abscess. (A) SE 500/40. The right CPA is obliterated. The IAC is normal. (W = 836, L = 327.) (B) SE 2000/80. The pathology is highlighted by T_2 weighting but the anatomical situation remains unclear. (W = 836, L = 327.) (C) IR 2000/500. The fourth ventricle is better defined. The lesion shows decreased signal. (W = 836, L = 327.) (D) Coronal IR 2000/500. The extra-axial component of this lesion is demonstrated (black arrows) and was confirmed at surgery. The IAC is normal (white arrow). (W = 779, L = 266.)

markedly prolonged T_1 (score -3). One meningioma showed a similarly increased T_1, but this appears to be atypical (Fig. 1A, B). In a larger series of meningiomas, including supratentorial lesions, we have found no other instance of such marked prolongation of T_1 (Mawhinney et al, 1986). It is interesting that when the meningioma in question was rescanned a year later, after surgery, recurrent tumour present showed considerable shortening of T_1, to within the range we have observed with other meningiomas (Fig. 1C).

The epidermoids were also of interest in showing contrasting T_1 values. Epidermoid cysts are filled with keratin, which would not be expected to produce shortening of T_1, but in a minority of cases the keratin in the cyst undergoes degeneration to produce a lesion containing large amounts of free, cholesterol-like lipid (Russel & Rubinstein, 1977). Such cases would consequently be expected to demonstrate shortening of T_1 as seen in one of our cases (Fig. 9). Latack et al (1985) reported one case of a calculated T_1 shortening from three cases studied but, in another review of 12 intracranial epidermoids, no increased tumour signal was observed on T_1-weighted SE sequences (Kortman & Bradley, 1985).

The finding of a low-signal lesion on IR sequences is therefore non-specific, though a very low signal is against a diagnosis of a meningioma. An increased signal on IR is considerably more useful, as it suggests either an epidermoid or a vascular lesion. In our case there was no reasonable doubt that the epidermoid was indeed a tumour. Where a vascular lesion is suspected, additional flow sequences can be performed to confirm the diagnosis (Fig. 5D).

Extension of tumour into the IAC is also supportive evidence for a diagnosis of neurilemmoma, but it is not specific (Fig. 7). We failed to identify extension in two cases where it was presumably present, based on CT findings of IAC widening. In these cases we did not define the canal on MRI. This is explicable on the basis that our scan protocol employs non-contiguous slices and the canal may therefore have fallen between cuts. The use of overlapping slices should overcome this problem.

As stated above, MRI has been shown to be superior to CT in the assessment of acoustic neuromas although CT probably remains superior to unenhanced MRI in defining posterior fossa meningiomas (Mawhinney et al, 1986). With respect to the remaining CPA lesions in this study, MRI was as good as or better than CT. In particular, the aneurysms were diagnosed with considerably greater confidence by MRI, while the epidermoids were more clearly identified and their anatomical relationships better defined by the multiplanar capacity of MRI (Figs 8 and 9).

REFERENCES

BRADLEY, W. G. & WALUCH, V., 1985. Blood flow: magnetic resonance imaging. *Radiology, 154,* 443–450.

BRADLEY, W. G., KORTMAN, K. E. & ZUNG, T. T. M., 1985. MRI of intracranial meningiomas. Presented at the IV annual meeting of the Society of Magnetic Resonance in Medicine, London. (Published by SMR, Berkeley, California.)

BYDDER, G. M., STEINER, R. E., THOMAS, D. J., MARSHALL, J., GILDERDALE, D. J. & YOUNG, I. R., 1983. Nuclear magnetic resonance imaging of the posterior fossa: 50 cases. *Clinical Radiology, 34,* 173–188.

BYDDER, G. M. & YOUNG, I. R., 1985. MR imaging: clinical use of the inversion recovery sequence. *Journal of Computer Assisted Tomography, 9,* 659–675.

Claveria, L. E., Sutton, D. & Tress, B. M., 1977. The radiological diagnosis of meningiomas, the impact of EMI scanning. *British Journal of Radiology, 50*, 15–22

Curati, W. L., Graif, M., Steiner, R. E., Kingsley, D. P. E. & Young, I. R., 1985. Further improvement of MRI sensitivity in the diagnosis of acoustic neuromas using Gd-DTPA. Presented at the IV annual meeting of the Society of Magnetic Resonance in Medicine, London. (Published by SMR, Berkeley, California.)

DeFilipp, G. J. & Buchheit, W. A., 1985. Magnetic resonance imaging of acoustic neuromas *Neurosurgery, 16*, 763–765

Hitselberger, W E. & Gardener, G., 1968. Other tumours of the cerebellopontine angle. *Archives of Otolaryngology, 88*, 712–714.

Kieffer, S. A., Binet, E. F. & Gold, L. H. A., 1975. Angiographic diagnosis of intra- and extra-axial tumours in the cerebellopontine angle. *American Journal of Roentgenology, 124*, 297–309.

Kingsley, D P. E., Brooks, G. B., Leung, A. W.-L. & Johnson, M. A., 1985 Acoustic neuromas: evaluation by magnetic resonance imaging *American Journal of Neuroradiology, 6*, 1–5.

Kortman, K. E & Bradley, W G, 1985. Magnetic resonance of epidermoid tumours Presented at the IV annual meeting of the Society of Magnetic Resonance in Medicine, London. (Published by SMR, Berkeley, California.)

Latack, J. T., Kartush, J. M, Kemink, J. L., Graham, M. D. & Knake, J. E, 1985. Epidermoids of the cerebellopontine angle and temporal bone: CT and MR aspects. *Radiology, 157*, 361–366

Mawhinney, R. R., Buckley, J. H., Holland, I. M. & Worthington, B. S., 1986. The value of magnetic resonance imaging in the assessment of intracranial meningiomas. *Clinical Radiology, 37*, 429–439.

Mikhael, M. A.; Ciric, I. S. & Wolff, A. P., 1985. Differentiation of cerebellopontine angle neuromas and meningiomas with MR imaging. *Journal of Computer Assisted Tomography, 9*, 852–856.

New, P. F. J., Bachow, T. B., Wismer, G. L., Rosen, B. R. & Brady, T. J., 1985. MR imaging of the acoustic nerves and small acoustic neuromas at 0.6 T. Prospective study. *American Journal of Neuroradiology, 6*, 165–170.

Olson, J. E., Glasscock, M. E. & Hill Britton, B., 1978. Lipomas of the internal auditory canal. *Archives of Otolaryngology, 104*, 431–436.

Rao, K. G. & Woodlief, R. M., 1979. CT simulation of cerebellopontine tumour by tortuous vertebrobasilar artery. *American Journal of Roentgenology, 132*, 672–673.

Russel, D. S. & Rubinstein, L. R., 1977. *Pathology of Tumours of the Nervous System*, 4th edit. (Edward Arnold, London).

Young, I. R., Bydder, G. M., Hall, A. S., Steiner, R. E., Worthington, B S., Hawkes, R. C, Holland, G. N. & Moore, W. S., 1983. The role of NMR imaging in the diagnosis and management of acoustic neuroma. *American Journal of Neuroradiology, 4*, 223–224.

Zimmerman, R. D., Fleming, C. A., Saint-Louis, L. A, Lee, B. C. P., Manning, J. J. & Deck, M. D. F., 1985. Magnetic resonance imaging of meningiomas. *American Journal of Neuroradiology, 6*, 149–157

Book reviews

Neuroanatomy and Cranial Computed Tomography Ed by H.-J. Kretschmann and W. Weinrich, pp. 168, 1986 (Georg Thieme-Verlag, New York), DM 198.
ISBN 0-86577-212-6 (New York)
3-13-672601-4 (Stuttgart)

The strength of this book lies in the beautifully drawn and presented diagrams of detailed anatomy and of functional anatomy of the various sensory and motor systems. The diagrams depict the distribution of the systems longitudinally and in sections made in the orbito-meatal plane commonly used for CT and transverse MRI.

Bony structures, CSF spaces, blood vessel anatomy distribution and supply as well as the internal structure of the brain are all described.

The effects of common lesions produced in various situations are briefly discussed; this serves to emphasise effectively their importance and impress the anatomical features upon the memory.

The authors do not reproduce actual CT or MRI images but use instead annotated tracings from them; this technique helps to emphasise particular features and does not detract from the sections as teaching material.

The book can be recommended for routine daily use in improving anatomical and functional localisation of lesions in radiological departments involved in cranial computed tomography. It provides the basic background knowledge essential for interpretation of CT sections, and the ease with which this can be assimilated from the excellent diagrams should appeal to both medical students and postgraduate neuroscientists studying this field.

BRIAN KENDALL

Functional Mapping of the Brain in Vascular Disorders Ed. by Wolf-Dieter Heiss, pp. 126, 1985 (Springer-Verlag, Berlin), DM 56.
ISBN 3-540-15801-4

This book is based on the proceedings of a symposium dealing with functional studies in cerebrovascular disease held in Hamburg in 1985. The principal techniques discussed are proton and sodium NMR imaging, phosphorus NMR spectroscopy, the use of PET with ^{15}O to detect uncoupling of flow and metabolism in brain ischaemia, pre-stroke, acute stroke and chronic infarction. The effects of focal ischaemia on the metabolism of distant parts of the brain and the study of synthesis using essential amino acids labelled with ^{11}C are presented

All of the contributors are invited experts in their fields; the papers are a review of both their personal work and the relevant literature, and each chapter is accompanied by a useful bibliography. The subjects are presented in a fashion suitable for non-experts to be able to appreciate the contribution of these complex methods to the fundamental understanding of metabolic processes *in vivo* and the practical implications in individual patients. The book is recommended to service neuroradiologists as an easy way of keeping abreast of progress in research in this field.

BRIAN KENDALL

Pocket Atlas of Cranial Magnetic Resonance Imaging. By V M. Haughton and D. L. Daniels, pp. 61, 1986 (Raven Press, New York), $14.00
ISBN 0-88167-171-1

This pocket atlas contains 52 labelled magnetic resonance (MR) images demonstrating normal anatomy of the brain in the transverse, coronal and sagittal planes. A single T_2-weighted spin-echo sequence using a high field system (1.5 T) has been selected for display and labelling of the normal anatomy. There is an insert of an inversion-recovery scan marked with a line indicating the plane of section for each image There is no text and the only figure captions relate to two spin-echo images with proton density-weighting shown for comparison. A few selected references are also given.

The image quality, as one would expect, is excellent, but the anatomical detail is somewhat limited and not enough to be of use to practising radiologists involved in MR scanning. It is a pity that comparative inversion-recovery images, which show more exquisite anatomical detail, were not selected as well. In general, T_2-weighted images are more sensitive for the detection of cerebral pathology, but inversion-recovery images have a place and should not be ignored.

In view of the limited availability of MR scanning in the UK at the present time, the greatest market for this atlas would be in the USA. However, it does elegantly display the multiplanar facility of MR imaging and would be useful to medical students, radiographers, interested clinicians and training radiologists as an aid to learning cerebral anatomy. The atlas, which has a strong plastic cover and binding, is good value.

J. P. R. JENKINS

The Cerebral Infarct: Pathology, Pathogenesis and Computed Tomography. By K.-J. Zülch, pp. 104, 1985 (Springer-Verlag, Berlin), DM 98.
ISBN 3-540-15866-9 (Berlin)
0-387-15866-9 (New York)

This book presents a series of photographs of brain sections which demonstrate the many and varied manifestations of brain ischaemia and infarction. Selected computed tomograms, made from a different series of patients but showing ischaemic lesions appearing very similar to those demonstrated by the pathological specimens, are used for correlation of the types of pathology which could be expected to underlie the CT appearances. Line drawings are effectively used to explain the pathogenesis of ischaemia, particularly emphasising the effects of arterial blockage or stenosis at various sites, and of collateral flow in influencing the production and siting of infarcts and of the border zones between arterial territories in which ischaemia occurs.

The author's extrapolations from pathology to computed tomographic appearances are so well expressed pictorially as to make the short text superfluous.

Professor Zülch's concepts are now widely accepted and the information obtained in this monograph will be familiar to neuroradiologists. Nevertheless, it is well presented and gives a firm basis for understanding the complexities of cerebral infarction and its CT manifestations, which should be particularly valuable to undergraduate and postgraduate students.

BRIAN KENDALL

1986, *The British Journal of Radiology*, 59, 971–973 OCTOBER 1986

A comparison of three methods for performing barium follow-through studies of the small intestine

By D. J. W. Morewood and G. H. Whitehouse

Department of Radiodiagnosis, University of Liverpool, Royal Liverpool Hospital, PO Box 147, Liverpool L69 3BX

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ABSTRACT

Domperidone 8 mg intravenously and metoclopramide 10 mg intravenously, in patients given a standard barium sulphate preparation, were compared with a rapid-transit barium (E-Z-Paque, E-Z-Em) in a double-blind random controlled manner. E-Z-Paque and metoclopramide given with a standard barium preparation decreased small-bowel transit time and resulted in fewer radiographs being taken. Gastric emptying occurred most rapidly with metoclopramide and a standard barium sulphate preparation. There was no significant difference in the quality or diagnostic accuracy of the examinations with any of the three techniques, and no difference in the incidence of side-effects with the two drugs.

Metoclopramide, an effective agent for increasing the rate of gastric emptying and stimulating intestinal peristalsis (Baeyens et al, 1979), is widely used in barium small-bowel studies to decrease the duration of what is often a lengthy procedure. However, metoclopramide acts centrally on the nervous system and occasionally has extrapyramidal side-effects, mainly in the form of dystonic reactions (Bretland, 1984). Death has been reported following a dystonic reaction due to metoclopramide (Casteels van Daele et al, 1984). Domperidone, a potent dopamine antagonist, has also been shown to increase the rate of gastric emptying and small-intestinal transit (Debontridder, 1980). Domperidone does not cross the blood–brain barrier and is, therefore, unlikely to cause extrapyramidal side-effects (Howarth et al, 1967), although there have been isolated case reports of domperidone causing dystonic attacks (James & Melrose, 1969; Reyntjens et al, 1978; Reasbeck & Hossenbocus, 1979). Death due to cardiac arrest has recently been reported with domperidone (Robinson, 1973a, b).

Baeyens et al (1979) compared the effects of domperidone and a placebo on gastric motility and emptying in patients referred for a barium follow-through examination. Domperidone, 8 mg intravenously, significantly promoted antral peristalsis and gastric emptying compared with the placebo. The results suggested that domperidone improved and synchronised motor function in the proximal part of the gastrointestinal tract. No adverse reactions were reported by Baeyens et al and extrapyramidal side-effects were absent.

E-Z-Paque (E-Z-Em) is a rapid-transit barium preparation containing 2% sorbitol by weight. The purpose of the sorbitol is to increase intestinal peristalsis by its osmotic effect.

The aim of the present study was to make a double-blind study of the efficiency of domperidone and metoclopramide in small-bowel meal studies and to compare both drugs with E-Z-Paque in respect of gastric emptying, small-intestinal transit time and the incidence of flocculation and dilution of the barium.

PATIENTS AND METHODS

Those patients attending the X-ray department for a small-bowel barium meal examination and who gave their informed consent were included in this study. The following categories of patients were excluded from the study: patients under 18 years of age, patients taking anticholinergic drugs, antidepressant drugs, metoclopramide or domperidone, patients with suspected intestinal obstruction, patients who had had previous surgery to the stomach or small intestine and those patients who had taken food or drink within the previous 9 h. After these exclusions, 99 patients were entered into the study. Their previous medical history, current medication and reasons for referral were recorded. These 99 patients were randomly allocated into three groups; one to receive 8 mg domperidone intravenously, the second 10 mg metoclopramide intravenously, both followed by 250 ml of barium sulphate suspension (Micropaque, Nicholas Laboratories). The third group received 250 ml of rapid-transit barium (E-Z-Paque) mixed to the 70% weight per volume recommended by the manufacturer.

Supine antero-posterior abdominal radiographs were taken every 30 min following the ingestion of the barium until the head of the barium column reached the ascending colon. At the end of the examination the patients given either domperidone or metoclopramide were asked about the presence or absence of the following symptoms during the investigation: nausea and vomiting; abdominal pain and, if present, the site and nature of the pain and whether it was the same or different from the presenting pain; the desire to defaecate and, if so, whether they experienced diarrhoea. The patients were asked specifically about extrapyramidal side-effects, namely rigors, hypokinesia, tremor, akathisia, oculogyric crises and dystonic reactions. The intensity of side-effects was graded as absent, present but not severe, and severe.

TABLE I

TIME TAKEN FOR BARIUM COLUMN TO REACH ASCENDING COLON AND THE NUMBER OF RADIOGRAPHS TAKEN, WITH PERCENTAGE OF PATIENTS IN EACH GROUP

Time (min)	No of radiographs	Domperidone and micropaque (%)	Metoclopramide and micropaque (%)	E-Z-Paque (%)
30	1	6	25	21
60	2	24	28	30
90	3	3	16	12
120	4	12	9	15
150	5	3	6	12
180	6	18	3	0
210	7	18	3	0
240	8	6	3	6
260	9	6	3	0
300	10	3	3	0
420	14	0	0	3

The amount of gastric emptying was empirically estimated on each of the radiographs as less than 50%, between 50 and 90% or over 90%. A record was made of the small-bowel transit time to the ascending colon. An overall assessment of the quality of the examination was rated as "poor", "moderate" or "good". Any abnormality demonstrated and the diagnosis established by the study were noted.

RESULTS

Of the 99 patients included in this study, 39 were male and 60 female. Thirty-three patients were assigned to each group. The mean age of the patients in the domperidone group was 43 years with a range of 22–74 years; 39 years in the metoclopramide group with a range of 20–70 years; and 51 years with a range of 19–81 years in the E-Z-Paque group.

The commonest reasons for referral were diarrhoea, suspected Crohn's disease and abdominal pain.

No patient complained of nausea or vomiting during the course of the examination. Four patients in the domperidone group and one in the metoclopramide group complained of abdominal pain during the examination. Of these, three in the domperidone group described the pain as identical to their presenting pain. The other patient in the domperidone group described the pain as mild and intermittent in nature, as did the patient in the metoclopramide group.

Two patients in the domperidone group and one in the metoclopramide group experienced a desire to defaecate during the examination, while one in the domperidone and two in the metoclopramide group experienced diarrhoea. One patient in the metoclopramide group experienced mild akathisia. No other extrapyramidal side-effects occurred in either group. No gastrointestinal symptoms followed the ingestion of E-Z-Paque.

The mean time taken for the barium to reach the ascending colon was 150 min in the domperidone group with a range of 30–300 min; 96 min in the metoclopramide group with a range of 30–300 min; and 99 min with a range of 30–420 min in the E-Z-Paque group. The mean time taken for the domperidone group was significantly different ($p < 0.05$ using the Mann–Whitney U-test), compared with the metoclopramide and E-Z-Paque groups. Fewer radiographs were taken in the metoclopramide and E-Z-Paque groups, because the mean transit time was less than that for the domperidone group. Table I shows the percentage of patients in each group, the number of radiographs taken and the transit times. Gastric emptying occurred most rapidly in the metoclopramide group (Table II). A gastric emptying of over 90% was present in all patients in the metoclopramide group at 90 min and at 210 min in the domperidone group and at 180 min with the E-Z-Paque group. The differences in the metoclopramide and domperidone groups was significant at 90 min ($p < 0.05$, Mann–Whitney U-test).

TABLE II

PERCENTAGE GASTRIC EMPTYING AT TIME INDICATED IN EACH GROUP

Time (min)	Percentage gastric emptying								
	< 50%			50–90%			> 90%		
	DOM	MET	E-Z-Paque	DOM	MET	E-Z-Paque	DOM	MET	E-Z-Paque
30	21	16	33	58	47	60	21	38	6
60	7	0	15	32	25	46	61	75	38
90	9	0	0	17	0	37	74	100	62
120	10	0	0	0	0	8	90	100	92
150	13	0	0	0	93	14	88	100	86
180	7	0	0	0	0		93	100	100
210	0	0	0	0	0		100	100	100
240	0	0	0	0	0		100	100	100
420									100

DOM = domperidone, MET = metoclopramide

The examination was considered of good quality in 27 patients given domperidone, 30 patients given metoclopramide and 29 patients given E-Z-Paque. A moderate quality of examination was assessed in five patients given domperidone, three given metoclopramide and four given E-Z-Paque barium. One study was considered to be of poor quality in the domperidone group.

The examination showed no abnormality in 31 patients given domperidone, 30 patients given metoclopramide and 31 given E-Z-Paque. In one patient given domperidone, Crohn's disease was present and another was deemed to have a malabsorption state. In one patient given metoclopramide, adhesions were demonstrated; Crohn's disease and backwash ileitis due to ulcerative colitis were demonstrated in another two patients. In the E-Z-Paque group, one patient had Crohn's disease and one had adhesions.

There was no significant difference in the incidence of flocculation or dilution of barium between the three groups. Flocculation of a slight degree occurred in no more than three patients in each group for any given time interval, and there was dilution of a slight degree in no more than four patients at any given time interval.

Discussion

Both domperidone, 8 mg intravenously (Debontridder, 1980) and metoclopramide (Robinson, 1973a, b; Roussak et al, 1984) have been shown to decrease small-bowel transit time in barium follow-through studies compared with placebo The present study, comparing these two agents and the barium preparation with added sorbitol, demonstrated a significant decrease in the length of time taken for barium to reach the ascending colon after metoclopramide with a standard barium sulphate preparation and in patients given the E-Z-Paque preparation, compared with those receiving 8 mg intravenous domperidone and a standard barium sulphate. To our knowledge, no other study has compared the efficacy of metoclopramide, domperidone and rapid-transit barium in small-bowel follow-through studies.

The fact that small-bowel transit time was significantly reduced in patients given metoclopramide and a standard barium sulphate or E-Z-Paque results in fewer radiographs being taken and, hence, a lower radiation exposure to the patient. There was no significant difference between the quality or diagnostic accuracy of the examinations using the two drugs or rapid-transit barium.

Gastric emptying occurred more rapidly in the metoclopramide group. There was no significant difference in side-effects between the two groups of patients given either drug. In particular, no neurological complications were encountered in this study.

Even though the small-bowel enema is now considered the definitive small-bowel radiological examination, many radiologists still perform small-bowel meal examinations (Sol et al, 1980). It is concluded that the examination is accelerated by using intravenous metoclopramide with a standard barium sulphate preparation or by giving E-Z-Paque, rather than intravenous domperidone, with the result that fewer radiographs are required with no decrease in the quality of the investigation.

REFERENCES

Baeyens, R., van de Velde, E., de Schepper, A , Wollaert, F & Reyntgens, A., 1979. Effects of intravenous and oral domperidone on the motor function of the stomach and small intestine. *Postgraduate Medical Journal, 55,* 19–23.

Bretland, P M., 1984 State of the art seminar: barium examination of the small bowel. *Journal of the Royal Society of Medicine, 77,* 435.

Casteels von Daele, M., Dobosz-Cyklis, R., van de Cassege, W., Verbreech, P. & Wijnaele, L , 1984 Refusal of further cancer chemotherapy due to antiemetic drugs. *Lancet, i,* 57.

Debontridder, O., 1980. Extrapyramidal reaction due to domperidone. *Lancet, ii,* 802

Howarth, F. H., Cockel, R. & Hawkins, C. F., 1967. Effect of metoclopramide upon gastric motility and its value in barium progress meals. *Gut, 8,* 635.

James, W. B. & Melrose, A. G., 1969 Metoclopramide in gastrointestinal radiography. *Clinical Radiology, 20, 57–60*

Reasbeck, P. G & Hossenbocus, A., 1979. Death following dystonic reaction to oral metoclopramide *British Journal of Radiology, 33,* 31.

Reyntjens, A. J , Niemegeers, C J. E., van Neuten, J. M., Laduron, P., Heykants, J , Schellekens, K H. L., Marsboom, R., Jageneau, A., Broekaert, A & Janssen, P. A. J., 1978. Domperidone, a novel and safe gastrokinetic antinauseant for the treatment of dyspepsia and vomiting. *Arzneimittel-Forschung, 28,* 1194.

Robinson, O. P. W., 1973a. Metoclopramide—a new pharmacological approach. *Postgraduate Medical Journal, 49, (Suppl. 4),* 9.

——1973b. Metoclopramide—side effects and safety. *Postgraduate Medical Journal, 49 (Suppl 4), 77.*

Roussak, J B., Carey, P. & Parry, H , 1984. Cardiac arrest after treatment with intravenous domperidone. *British Medical Journal, 289,* 1579

Sol, P., Pelet, B. & Guignard, J. P., 1980. Extrapyramidal reaction due to domperidone. *Lancet, ii,* 802.

Book reviews

Radiologic Diagnosis of Renal Transplant Complications. By W R. Castañeda-Zuñiga, pp 306, 1986 (University of Minnesota Press, Minneapolis), $49.50.
ISBN 0-8166-1232-3

This is a useful book by 16 contributors, 12 of them from Minnesota. These ties among the authors must have helped toward achieving an integrated approach. The scope of the volume is quite wide: 11 chapters beginning with chest radiographs and ending with interventional techniques. There are, inevitably, local characteristics to colour the picture; thus, we learn in the nuclear medicine chapter that splenectomy has been a routine in renal transplants at the University of Minnesota for many years. Interesting and unexpected corners of the field are covered, for instance, echocardiographic studies to show that abnormalities of left-ventricular mass begin to regress immediately after an operation. The authors say practical and honest things like "routine angiography has proved to be of little value when rejection is suspected" and "important limitations to the ultrasonographic evaluation of acute and chronic rejection should be noted".

I found this a well illustrated and helpful book which should interest radiologists involved with renal transplantation.

Thomas Sherwood

Essentials of Nuclear Medicine Imaging, 2nd edit. By Fred A. Mettler Jr and Milton J Guiberteau, pp xviii+380+index, 1985 (Grune & Stratton, New York), $47.50.
ISBN 0-8089-1767-6

This is the second edition of an introductory text which should be of value to trainee nuclear medicine physicians, radiologists and nuclear medicine radiographers. Several chapters have been updated to bring the contents abreast of recent developments. While it is inevitable that many topics are dealt with only briefly, the authors have successfully outlined the broad spectrum of nuclear medicine with no serious omissions. The style of writing is clear and coherent and the text and illustrations are well presented. There are, however, several surprising misprints, the first of these being in the first line of the preface!

The first 60 pages of this 380-page book are devoted to the basic principles and hardware of nuclear medicine This is a concise and eminently readable section but most trainees would find the short list of references at the end of each chapter to be essential supplementary reading. The clinical sections place the emphasis on the practical application of nuclear medicine techniques and there are useful warnings on the common pitfalls to be avoided in interpretation. The final chapter discusses legal requirements and radiation safety, much of which is not directly applicable outside the United States. Despite the introductory nature of this volume, a more comprehensive account of radiation hazards and safety would have been valuable. There are the usual appendices detailing the commonly used radionuclides and techniques, together with a useful summary of the radiation dose to the fetus from imaging during pregnancy.

In conclusion, this book has been well received by both doctors and radiographers training in this department, and would be a useful addition to the library of any department of nuclear medicine with a teaching commitment.

V. B. Batty

Joints and Vertebral Connections By W. Dihlmann, pp. 580, 1985 (Thieme Inc, New York), DM.168.
ISBN 0-86577-161-8 (New York)
3-13-660401-6 (Federal Republic of Germany)

What a pity! Wolfgang Dihlmann has written a truly magnificent textbook of bone and joint radiology, for which he should be congratulated The whole concept of regional disease illustrated by numerous high quality line drawings is most appealing. The succinct, clear diagrams emphasise the main features of disease which are, perhaps, more easily comprehensible from this medium than from the usual alternative of less than perfect reproductions of radiographs. Unfortunately the book is unreadable by most of us because of its translation. The difficulty is not just a matter of German-English vocabulary. It is, I fear, compounded by a different concept of disease nomenclature and classification between our cultures. Nonetheless, I am sure that this is a very excellent book which cannot be appreciated to its full in this edition, but will be a gem when revised. I believe it could have been a book very much needed in our libraries As I said to begin with, what a pity!

Iain Watt

Correction

Fundamentals of Nuclear Medicine Handbook of Nuclear Medicine, Vol. 1/1. Ed. by H Kriegel, pp. 515, 1985 (Gustav Fischer Verlag, Stuttgart), DM324 ISBN 3-437-10828-X

Please note that the price of the above book, reviewed in the January 1986 issue of the Journal (p 91), was incorrectly quoted as DM19 80 Please would readers correct their copies

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Multiple-section radionuclide tomography of the kidney: a clinical evaluation

By E. D. Williams, Ph.D., F.Inst.P., *C. Parker, F.R.C.S., D. Rankin, M.B., B.S.
and *R. R. Roy, F.R.C.S.

Regional Medical Physics Department, Sunderland District General Hospital and *Urology Department,
Royal Infirmary, Sunderland

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ABSTRACT

The clinical utility of radionuclide emission tomography of the kidney in comparison with conventional gamma-camera imaging has been assessed from scans of 60 patients suspected of having space-occupying lesions of the kidney. Nineteen patients had renal tumour, 17 had cysts and seven had renal pseudotumours; the remainder had no lesion. Objective trials using four observers showed only a slight, statistically insignificant advantage from the addition of tomographic sections to conventional images. However, in several individual cases tomography had aided diagnosis, particularly in obese patients, when an alternative non-invasive investigation (ultrasonography) was inconclusive. In seven patients a positive diagnosis of renal pseudotumour was made possible by tomography, definite identification of ectopic functioning cortical tissue at the location of a mass suspected after urography was considered to be a distinct diagnostic advantage gained from emission tomography of the kidney.

Rotating gamma-camera systems for multiple-section radionuclide emission computed tomography have recently become generally available. Such systems offer the possibility of improved lesion detection compared with conventional radionuclide imaging and this has been demonstrated in studies of brain (Ell et al, 1980) and liver (Khan et al, 1981). Improved detection of defects in uptake has been obtained in investigations of the myocardium (Tamaki et al, 1984), and it is, therefore, possible that the same advantages in depicting functional morphology (Laird et al, 1984) apply to the kidney. The time required for satisfactory imaging by emission tomography appears to preclude dynamic studies of renal function with a rotating gamma camera and currently accepted amounts of administered radioactivity. The use of tomography for detection and localisation of lesions is, therefore, a more suitable area of investigation (Botsch et al, 1982; Williams et al, 1982, 1984). For the kidney, clinicians can now often choose radionuclide imaging, ultrasonography or computed tomography from non-invasive investigations to evaluate space-occupying lesions suspected clinically or detected on excretion urography (O'Reilly et al, 1981). However, computed tomography is not readily available in all district general hospitals, so improvements to radionuclide imaging techniques may yet have a part to play in diagnosis.

This study was carried out in order to determine as objectively as possible whether the additional information obtained from multiple sections could aid detection and localisation of space-occupying lesions of the kidney. The radiopharmaceutical we used was ^{99}Tc^{m}-DMSA, which is taken up by the renal cortex (Bingham & Maisey, 1978) and is advised for use in investigating possible renal masses (Maisey, 1980).

PATIENTS

Sixty patients were studied in whom space-occupying lesions had been suspected, in most cases on the basis of findings from intravenous urography, and in whom further non-invasive investigations were required. The only additional selection was the exclusion of patients with impaired overall renal function resulting in poor uptake of radioactivity in the kidneys. Sixty-three sets of radionuclide scans were consequently obtained (three of the patients each having two scans) and these form the main body of data for this study. All patients had two functioning kidneys and normal overall renal function. Nineteen patients had a renal tumour involving a kidney, one of these also having a renal cyst, and one patient had a second scan. Seventeen patients had renal cysts, five of these having two cysts, and one had a second scan. Seven patients had renal pseudotumours (*i.e.* a hypertrophied column of Bertin, or cortical nodule) and in one the scan was repeated. In 17 patients no renal lesion was found. The repeated scans were obtained several months after initial scans, and their inclusion is considered justified because differences in positioning resulted in sets of images which were not identical in appearance. An additional 11 sets of scans obtained similarly from other patients not included in the study group were used for training observers, as described below.

METHODS

All the patients in the study series had excretion urography, usually before radionuclide imaging. All also had an ultrasound examination performed with knowledge of other findings available at that time, usually those of urography and planar radionuclide imaging. Ultrasound scanning was carried out using

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Correspondence address: Dr E. D Williams, Regional Medical Physics Department, Sunderland District General Hospital, Kayll Road, Sunderland SR4 7TP.

both a linear-array real-time scanner (Toshiba SAL-20) and a B-mode scanner (Diasonograph 4200). Where appropriate, findings were confirmed at operation (usually the case for renal tumours) or, in a few cases, by angiography or biopsy. In other cases, where no lesion was confirmed when the other non-invasive techniques were applied, clinical follow-up for at least 1 year without further relevant symptoms was obtained and this was considered sufficient to reduce substantially the possibility of a missed renal tumour. Renal cysts were identified by a non-invasive procedure (ultrasound); invasive investigations were not considered to be justified in such cases. The patients judged to have a pseudotumour were so classified by careful comparison of the urogram, ultrasound scan and radionuclide tomogram, and by clinical follow-up. In a few cases ultrasound scanning was repeated, and one of these patients had selective renal angiography.

Imaging

Each patient was given an intravenous injection of 100 MBq ^{99}Tc^{m}-DMSA. The DMSA was used freshly prepared to ensure high renal specificity (O'Reilly et al, 1979). Conventional gamma-camera imaging was carried out 3 h after injection, using a large-field gamma camera (IGE 400T Maxicamera in earlier studies and IGE 400AT in later studies). A low-energy, general-purpose collimator was used and kidney images each of 500 000 total counts obtained in posterior and left and right posterior oblique views. Images were recorded directly from the gamma-camera display using Kodak NMB transparency film.

Tomographic imaging was then carried out using the same gamma camera and collimator, with data acquisition for 20 s at each of 64 positions over 360° around the patient. The radius of rotation was normally 20 cm, but in a few cases had to be increased to accommodate obese patients, although it was never more than 25 cm. Under these conditions the spatial resolution was about 19 mm full width at half maximum. Tomographic data were acquired in a 64×64 matrix using a Gamma-11 computer system (Digital Equipment Co.), the pixels having 6.1 mm sides, and transverse slices 2 pixels thick were reconstructed using the SPETS system (Larsson, 1980). Sagittal and coronal sections were also reconstructed orthogonal to the transverse sections, the thickness of each of these sections also being 2 pixels. Images were interpolated into a 128×128 matrix, displayed with 10% background subtraction on a monochrome video monitor (Tektronix Type 634) and photographed using Kodak GRS film.

Reporting

Conventional and tomographic images were compared by observer trials following the general methods described by Swets and Pickett (1982). For the purposes of this study, images were reported blind, that is, without additional information being supplied from other investigations or clinical history. Four observers were used, working separately. Each was asked to report the series of conventional kidney images and then, on a separate occasion at least 1 week later, to report the tomographic sections in conjunction with the corresponding conventional images. The viewers were on each occasion first given "a training set" of 11 scans, on which the test administrator pointed out relevant features, including the orientation of tomographic sections. Transverse, sagittal and coronal sections were all presented together because earlier work (Williams, 1983; Williams et al, 1983) has suggested that sagittal and coronal sections were often considered subjectively to be more useful than transverse sections; the most useful planes did, however, vary from case to case. All observers were accustomed to reporting radionuclide images, but only two were familiar with renal tomograms. Tests were carried out under normal reporting conditions, usually in the observer's own room, using a light box for illumination of the films. Observers were allowed as much time as they felt necessary to come to a decision about each scan, and on average this was about 1 min in the case of conventional scans and about 2 min when tomographic scans also were provided. Sets of images were presented in random order and the order of presentation was changed between the two sessions. One observer later repeated reporting of the conventional image set and another repeated the set of tomogram images to assess reproducibility.

The observers were asked to report each set of scans on the following scale (Swets & Pickett, 1982): 1 (normal), 2 (probably normal), 3 (equivocal, possibly abnormal), 4 (probably abnormal) and 5 (definitely abnormal). In those cases given ratings 2–5, the observer was asked also to give the location of the lesion: in the right or left kidney and in the upper, middle or lower part of that kidney. Observers were warned in advance that in some cases there was more than one lesion in a pair of kidneys and that the series included some cases of pseudotumour, which give ectopic uptake of radioactivity, quite different from cysts and solid tumours, which give defects in the normal uptake pattern.

DATA ANALYSIS

From all the clinical and diagnostic information available, each set of scans was assigned to a diagnostic group which was either normal, *i.e.* with no evidence of a space-occupying lesion in either kidney, or had evidence of tumour, cyst or pseudotumour. The location of each lesion was specified as upper, middle or lower third of the kidney and the mean of the available data was used to provide an estimate of its size. The observers' reports were compared with this objective diagnostic information to construct receiver operating characteristic (ROC) curves (Metz, 1978). Curves were constructed for each observer for both reporting situations, *i.e.* with conventional scans only and with tomographic sections also available. First, "detection

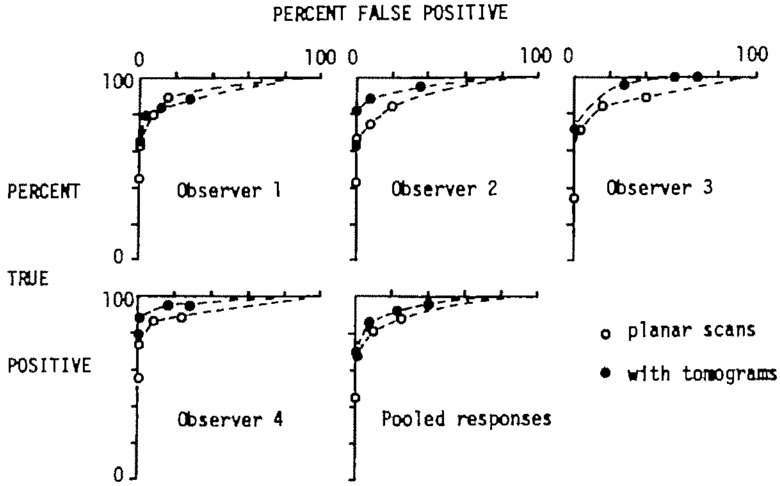

Fig. 1

Receiver operating characteristic (ROC) curves for the four observers for detection of renal lesions on planar images and with tomograms. The curve for the pooled responses of all observers is also shown.

task" curves were constructed, in which all information concerning number and location of lesions was ignored, and only the presence of at least one reported lesion on a set of scans was considered to give a "positive" scan report. Second, localisation ROC (LROC) curves were constructed (Starr et al, 1975), for which a response was considered correct "true positive" only if both the kidney in which a lesion was located was identified and the appropriate part of the kidney specified. Some latitude was allowed in the localisation, in that either the correct part or the adjacent part of the kidney was permitted as a correct response. Thus, a lesion in the upper third of the left kidney was considered to be correctly identified if the observer reported a lesion in either the upper or middle third of the left kidney.

In order to compare the ROC curves derived from the observer trials for "conventional" and "with tomogram" images, so as to determine whether tomograms provided any advantage, parameters were derived from each set of ROC data. These parameters were the area under the curve and its standard error, and they were obtained from a maximum-likelihood fit of the data using the computer program of Dorfman and Alf (1969) as given by Swets and Pickett (1982). In a few cases this approach failed to fit the data and another computer program based on the use of trapezium rule integration (Hanley & McNeil, 1982) was employed. The ROC curves for each observer for the two imaging techniques were then compared following the methods of Hanley and McNeil (1983). Comparison was also made using average ROC parameters for all observers. Averaging was carried out in two ways: by averaging the derived ROC indices (area, SE) for each observer and by pooling all test responses before constructing the ROC curve. Account was taken of the effect on comparison of ROC indices of using the same observers for all reporting (Swets & Pickett, 1982; Hanley & McNeil, 1983).

Results

Lesion detection

The ROC curves for the four observers are shown in Fig. 1 for the detection task. For three out of the four observers the ROC curves show apparently improved accuracy for scans with tomographic sections, compared with those without, and for the fourth

TABLE I

Detection of lesion on scans. comparison of ROC curve parameters

	Planar scans		Planar plus tomograms		At–Ap	SE of difference	Critical ratio*
	Area under ROC (Ap)	SE	Area under ROC (At)	SE			
Individual results							
Observer 1	0.940	0.035	0.914	0.044	−0.026	0.046	−0.57
Observer 2	0.889	0.055	0.949	0.033	0.060	0.049	1.22
Observer 3	0.897	0.044	0.945	0.025	0.054	0.040	1.34
Observer 4	0.925	0.035	0.962	0.025	0.037	0.040	0.92
Averages							
Averaged indices	0.913	0.042	0.942	0.032	0.030	0.034	0.88
Pooled responses	0.911	0.022	0.943	0.016	0.032	0.023	1.40

* Critical ratio denotes significance (as for *t*-statistic) and = difference in areas under ROC/SE of difference.

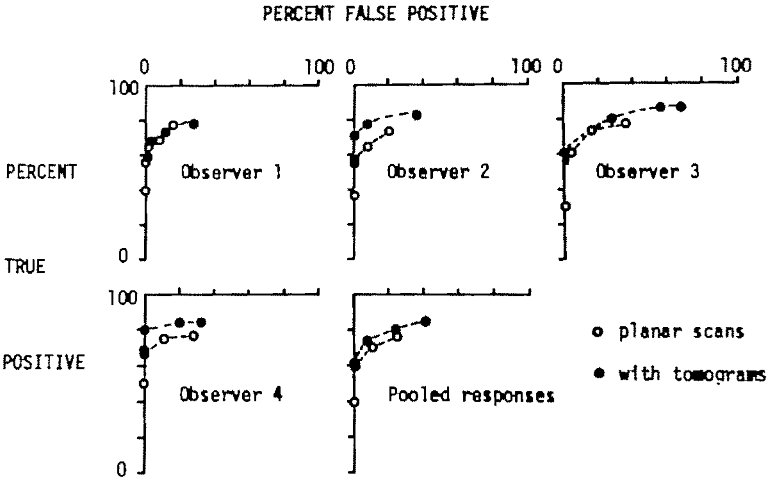

FIG 2.

Localisation ROC curves for the four observers and their pooled responses, for detection and correct localisation of renal lesions.

observer there is no difference in results. However, when the areas under the ROC curves were submitted to tests for significance (Table I), there was no significant difference between test results obtained with and without tomograms, nor when averaged ROC indices or pooled response results for all the observers were compared.

Lesion localisation

The LROC curves for the four observers are shown in Fig. 2. These curves are generally similar to those for detection ROC, but with lower true positive fractions. There is no sound basis for testing the significance of any difference between these curves, but theoretical considerations link them closely to detection ROC (Swets & Pickett, 1982). It is suggested that LROC curve data may best be compared by quoting the true positive fraction for a 10% false positive rate. These values, obtained by linear interpolation, are given in Table II and suggest a small improvement when tomograms were used, although this fails to reach conventional levels of significance (by *t*-tests).

Lesion size and type

The relationship between the size, nature and location of the lesions and the proportion detected was examined. For this purpose only reports with scores graded as 4 or 5 were considered (probably or definitely abnormal: in practice, the categories which would be reported to a clinician as being abnormal). For lesions detected using this criterion, on planar views 60% of lesions were detected, averaged over the four observers, whereas when tomography was added 74% were detected ($p < 0.01$, *t*-test) (Table III). These percentages correspond to the sensitivities of the techniques. There was a similar increase in detection rate for cysts and for tumours, indicating that there was no qualitative difference in any improvement in detectability gained with tomography for these two types of lesion. Lesion size, however, did appear to affect detectability. Figure 3 shows the percentage of "true positives" detected and located plotted against lesion size grouping. The probability of detection thus appears to increase with lesion size and was 100% for tomographic scans of lesions greater than 60 mm across.

TABLE II

LOCALISATION ROC: COMPARISON OF TRUE POSITIVE RATES AT 10% FALSE POSITIVE RATE (DETERMINED FROM ROC CURVES)

	% True positive	
	Planar	Planar plus tomograms
Observer 1	70	72
Observer 2	66	77
Observer 3	67	68
Observer 4	74	82
Mean	69	75

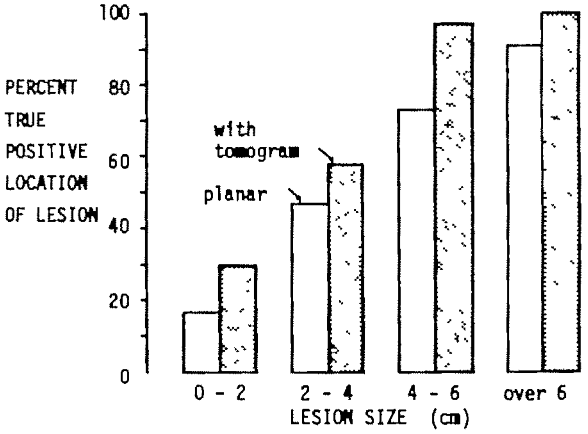

FIG. 3

Percentage true positive (rating 4 or 5) scans for detection and localisation was higher for the larger lesions, and slightly higher when tomograms were added.

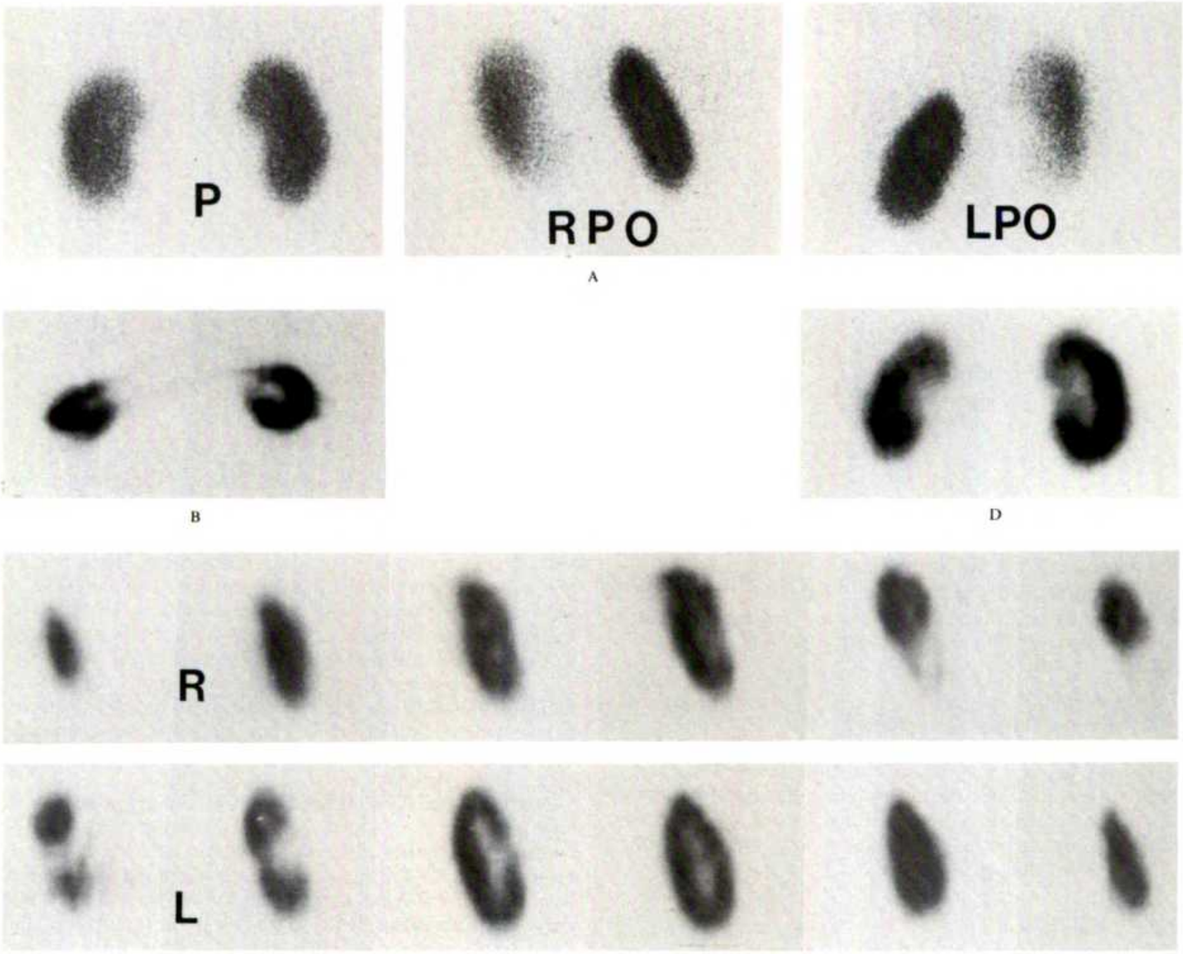

FIG. 4. *Case 1.*

(A) Normal planar views, (B) transverse, (C) sagittal, and (D) coronal tomographic sections. Note that following convention, planar scans are shown as posterior views, but coronal sections as anterior views. Sagittal sections are viewed from the right lateral position, with the patient's anterior on the right. Transverse sections are as viewed from the patient's feet, with anterior at the top of the picture. P, posterior, left and right as shown; RPO, right posterior oblique; LOP, left posterior oblique, and in subsequent Figs.

TABLE III

NUMBER OF LESIONS "DETECTED" (SCORE 4 OR 5) ACCORDING TO TYPE (CYST OR SOLID TUMOUR)

	Cyst ($n = 24$)		Tumour ($n = 20$)		All lesions ($n = 44$)	
	Planar	Tomo	Planar	Tomo	Planar	Tomo
Observer 1	11	14	13	16	24	30
Observer 2	12	15	13	16	25	31
Observer 3	13	17	14	18	27	35
Observer 4	15	16	14	19	29	35
Mean	12.8	16.5	13.5	17.2	26.2	32.8
% of total	53	69	68	86	60	74

Tomo = planar + tomograms.

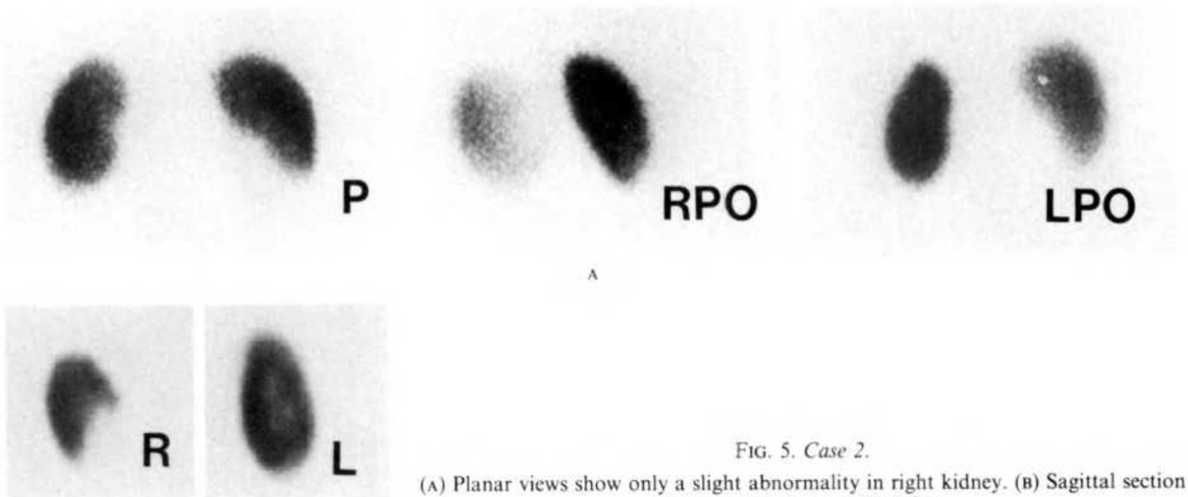

FIG. 5. *Case 2.*

(A) Planar views show only a slight abnormality in right kidney. (B) Sagittal section shows a clear lower-pole defect.

CASE EXAMPLES

As examples of the usefulness of tomographic imaging and the relationship of the results to those obtained by other investigations, the following cases are cited.

Case 1: normal

A 53-year-old man was thought, on the basis of his urographic examination, to have a renal lesion. Conventional, transverse, sagittal and coronal sections showed uptake in renal cortex only and no distortion or defects (Fig. 4). No lesion was subsequently demonstrated by any other imaging technique, and there was no evidence of any renal abnormality on subsequent clinical follow-up.

Case 2: renal tumour

A 57-year-old man had no renal symptoms but a chest radiograph showed two rounded opacities in the peripheral left lung. A subsequent excretion urogram showed fullness of all the calyceal groups in the right kidney, which were pressed upwards, presumably by a lower-pole mass. The scan (Fig. 5) showed some reduced uptake in or distortion of the right kidney, but no clear defect. However, sagittal tomographic sections clearly indicated a right lower-pole defect, which was also visible, but less clearly, on coronal sections. Ultrasound indicated that this was due to a solid mass and at subsequent nephrectomy a clear-cell renal adenocarcinoma was removed.

Case 3: renal tumour

A woman aged 57 years presented with urinary infection and right loin pain for 6 months. An excretion urogram showed the medial border of the lower pole of the right kidney to be slightly enlarged and the lower-pole collecting system to be distorted. A planar $^{99}Tc^{m}$-DMSA kidney scan showed only an indistinct area of reduced uptake in the lower pole of the right kidney, but coronal and sagittal tomograms (Fig. 6) revealed a clear defect. The ultrasound scan was of poor quality owing to the patient's obesity and no lesion could be identified. Subsequently, a solid

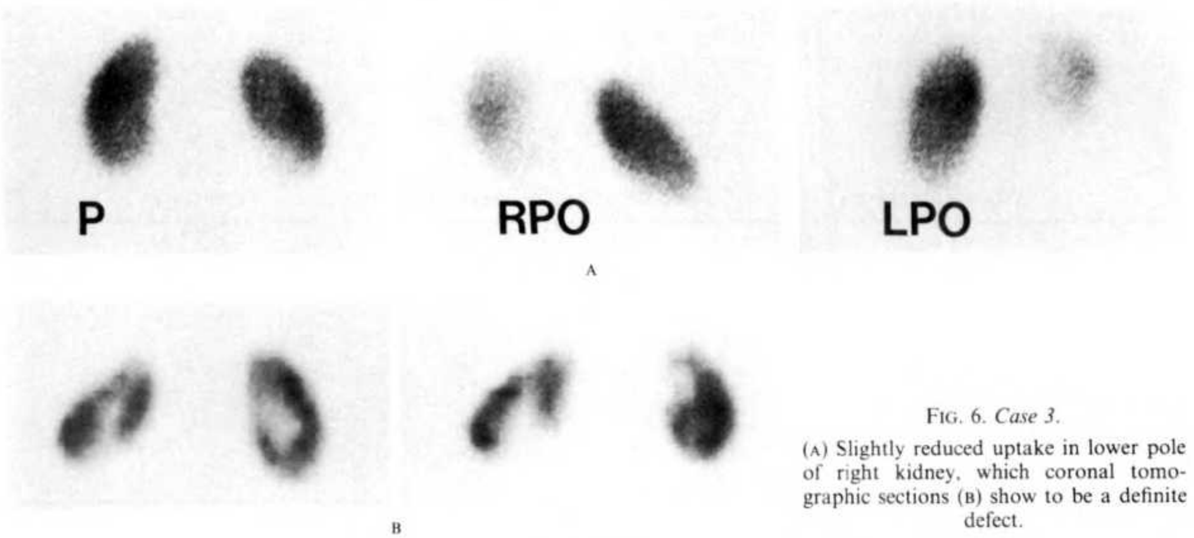

FIG. 6. *Case 3.*

(A) Slightly reduced uptake in lower pole of right kidney, which coronal tomographic sections (B) show to be a definite defect.

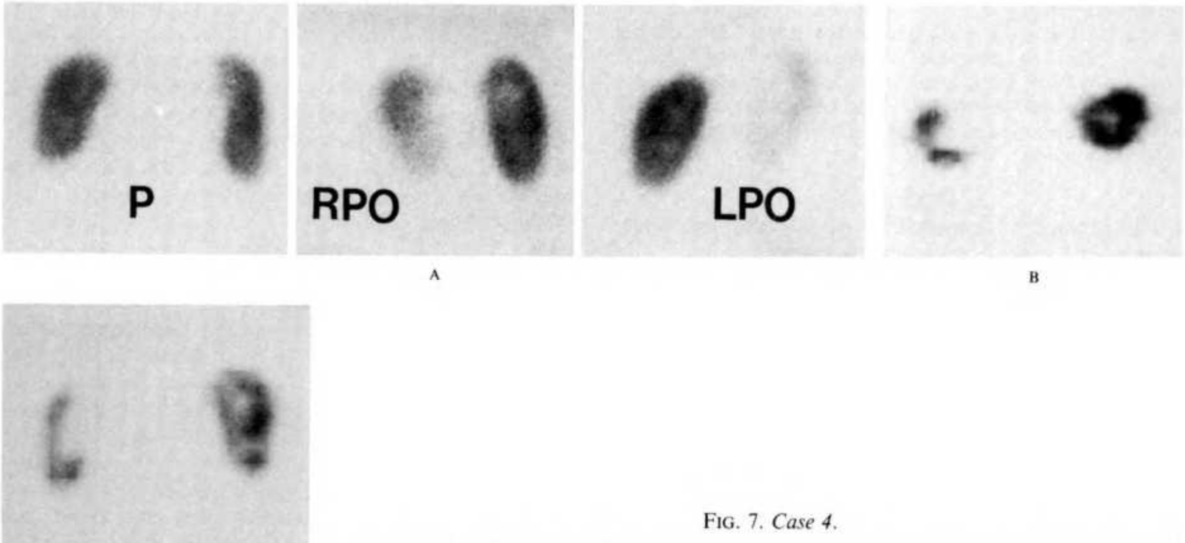

FIG. 7. *Case 4.*

(A) Possible right upper-pole lesion on conventional scan. (B) Transverse and (C) coronal sections show a defect in medial aspect of upper pole.

tumour was demonstrated by angiography and confirmed at surgery. (This case is also described by Jarritt and Ell (1984) and wrongly attributed to another institution.)

Case 4: angiomyolipoma

A woman aged 75 years with an unstable bladder and urinary tract infection was investigated by excretion urography, which indicated a mass, possibly a cyst, in the upper pole of the right kidney. A ^{99}Tc^{m}-DMSA scan (Fig. 7) also suggested a possible right upper-pole lesion, but there was no definite parenchymal defect visible. Transverse and coronal tomograms showed that the upper pole of the right kidney was expanded, and absence of any uptake on its medial side suggested the presence of a mass projecting medially from the kidney. Ultrasound scanning was technically inadequate on account of the patient's obesity and, while consistent with a solid mass projecting medially from the upper pole of the right kidney, neither the extent of the mass nor its existence could be firmly determined. A CT scan showed a mass medial to the upper two-thirds of the right kidney, which contained fatty tissue, and was presumed to be an angiomyolipoma. Surgery was not carried out and repeated investigations 1 year later showed no change.

Case 5: pseudotumours

A 62-year-old man presenting with abdominal pain underwent several investigations including urography, which showed compression of the calyces of the right kidney, indicating a possible renal mass. An ultrasound scan showed solid tissue in the middle of the right kidney, with echogenicity similar to normal renal parenchyma. In the left kidney there was a similar but smaller area. A ^{99}Tc^{m}-DMSA scan was

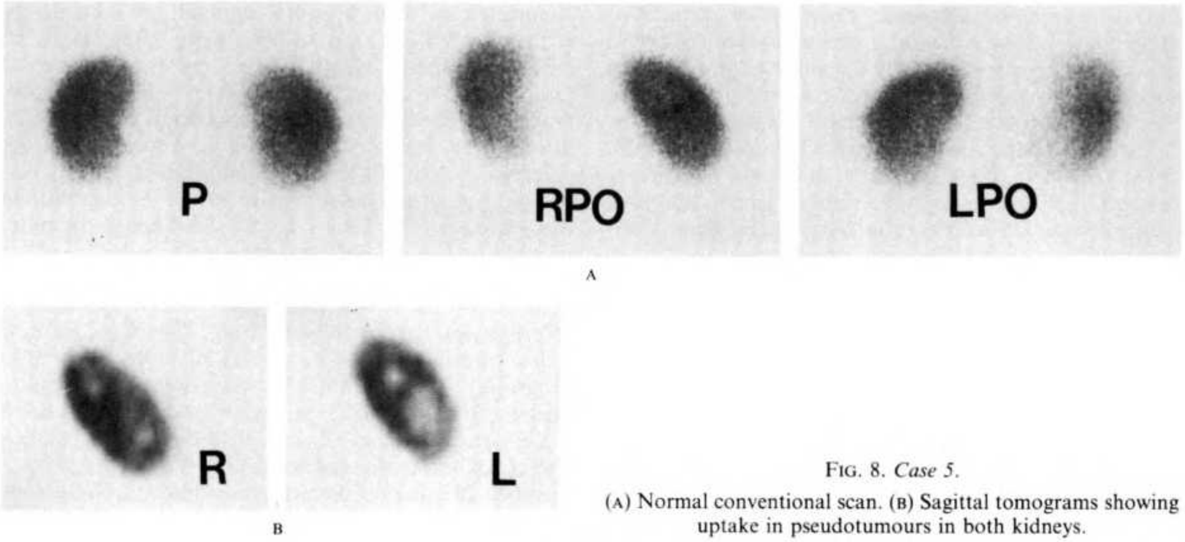

FIG. 8. *Case 5.*

(A) Normal conventional scan. (B) Sagittal tomograms showing uptake in pseudotumours in both kidneys.

normal on conventional views (Fig. 8), but sagittal sections showed a large area of uptake in the middle of the right kidney, extending from the dorsum, and a much smaller similar area in the left kidney Appearances were considered to show renal pseudotumours and clinical follow-up and repeated investigations showed no change and no evidence of any other renal abnormality.

Discussion

The addition of tomographic sections did not appear to provide a general improvement in the detectability of renal space-occupying lesions in this series of patients, compared with the information present in conventional planar views alone, when assessed by an objective observer trial. From the variance of data obtained in the observer trials, it is possible to say that if there was a 10% advantage in "accuracy" (as measured by the area under the ROC curve) resulting from the use of tomograms, then this would have been detected and appeared statistically significant.

However, in clinical use we have found advantages in specific cases, as illustrated in this paper, which were a relatively small proportion of the total in our unselected series. Therefore, we consider that with appropriate selection of patients, tomography can provide useful diagnostic information. In selecting appropriate cases it is necessary to base a judgment on the results of other investigations, and it is difficult to apply such a process and still carry out an objective ROC analysis. There are two reasons why this was not attempted. One is that the ROC analysis is inappropriate for the very small number of data sets we would have if the only patients selected were those very likely to have the diagnosis affected by the results of tomography. Involved in such a selection is the second reason, which concerns the influence, varying from one case to another, of the results of other tests or clinical history. If all such information is given to each observer in a trial, it is difficult to determine to what extent one procedure, such as tomography, influences the final diagnosis. A possible alternative approach which takes account of these other factors is Bayes' procedure which, however, would be inappropriate for producing an objective conclusion in the circumstances presented here, since the prior probability of disease depends on the constitution of the patient population considered (Shea, 1978). We have, therefore, used ROC analysis, taking conventional and tomographic images in isolation, to compare how the information provided by them alone can contribute to the diagnostic process.

A major defect in the information obtained by the radionuclide imaging procedures described is that renal lesions may be detected but not characterised. The addition of a series of perfusion images (O'Reilly et al, 1981) can aid characterisation, particularly for the larger lesions, since a vascular mass generally indicates a solid tumour. However, this sign is often not found even when a tumour is present, and in any case such data were not available for many of the cases reported here. Ultrasonography was clearly a better procedure than radionuclide imaging for detecting renal cysts and is well established as a means of characterising them (Sherwood, 1975): in this series, radionuclide tomography had 86% sensitivity for tumours, but only 65% for those cysts detected by ultrasound. In practice, higher figures than these for correct localisation and identification of renal masses can be achieved, because information from other investigations is usually available at the time of reporting.

One area of diagnosis where we have found tomographic images to be particularly useful has been in the positive identification of renal pseudotumours (Williams & Parker, 1982). These can mimic renal tumours or cysts on urography (Feldman et al, 1978; Thornbury et al, 1980) and, while conventional radionuclide imaging is recommended in such circumstances (Grossman et al, 1983), the finding of a normal radionuclide conventional scan clearly does not rule out a lesion, and arteriography may be considered necessary (Lams et al, 1979). Our observers, reporting blind, did badly in picking out the pseudotumours from the rest of the scans, none being detected and reported as such on the conventional images, while on tomographic sections one observer found one pseudotumour (out of eight such sets of scans) and another observer found three. However, as noted above, in clinical practice, scans would usually be interpreted with the aid of information from urography and ultrasonography (Mahoney et al, 1983) and under such circumstances we have been able to match findings from the various techniques to identify this benign normal variant in each of the seven cases included in this series.

We have also found tomographic imaging useful in investigating obese patients, in whom ultrasound images are often of poor quality. While in such cases the substantial difference in ultrasonic image characteristics between a cyst and normal renal tissue makes detection and characterisation still relatively easy, the same is not true for solid tumours, which, in these circumstances, can be very difficult to identify by ultrasonography. Thus, tomography may then be particularly useful, *e.g.* in Cases 3 and 4, where a renal tumour in an obese patient was revealed by tomography. In these cases conventional scans were normal, or nearly so, because the lesion was so located that the defect in uptake was hidden. Radionuclide imaging was then an important non-invasive means of establishing the presence of a lesion before progressing to more invasive or less readily available investigations

Selection of patients for emission tomography of the kidney can be made after the other non-invasive investigations have been carried out. Therefore, we now follow the advice of O'Reilly et al (1981) and after urography proceed to ultrasonography and radionuclide imaging, with a perfusion study. At that point the information from all these investigations is collated and compared to determine whether a clear diagnosis is possible. If it is not, then emission tomography can be carried out, its primary role being either to identify a possible lesion as a pseudotumour or to confirm or disprove the presence of a lesion. Thus, we can determine whether it is necessary to proceed to computed tomography or angiography.

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REFERENCES

Bingham, J. B. & Maisey, M. N., 1978. An evaluation of the use of ^{99}Tc^{m}-dimercaptosuccinic acid (DMSA) as a static renal imaging agent. *British Journal of Radiology, 51,* 599–607.

Botsch, H., Pottmeyer, A., Savaser, A., Lochner, B. & Banzer, D., 1982. Emission tomography with 7-pinhole collimator for kidney imaging. In *Radionuclides in Nephrology*. Ed. by A. M. Joekes, A. R Constable, N. J. G. Brown & W. N. Tauxe (Academic Press, London), pp. 83–86.

Dorfman, D. D & Alf, E., 1969. Maximum-likelihood estimation of parameters of signal-detection theory and determination of confidence intervals—rating-method data *Journal of Mathematical Psychology, 6,* 487–496.

Ell, P. J., Deacon, J. M., Ducasson, D. & Brendel, A., 1980. Emission and transmission brain tomography *British Medical Journal, 280,* 438–440.

Feldman, A. E., Pollack, H. M., Perri, A. J., Karafin, L. & Kendall, A. R., 1978. Renal pseudotumours: an anatomic-radiologic classification. *Journal of Urology, 120,* 133–139.

Grossman, Z D., Ellis, D. A. & Brigham, S. C, 1983. *The Clinician's Guide to Diagnostic Imaging* (Raven Press, New York), p. 63.

Hanley, J. A. & McNeil, B. J., 1982. The meaning and use of the area under a receiver operating characteristic (ROC) curve. *Radiology, 143,* 29–36.

Hanley, J A. & McNeil, B. J., 1983. A method of comparing the areas under receiver operating characteristic curves derived from the same cases. *Radiology, 148,* 839–843

Jarritt, P H. & Ell, P. J., 1984 *Gamma Camera Emission Tomography* (Current Medical Literature, London), pp 146–147.

Khan, O, Ell, P. J., Jarritt, P. H., Cullum, I. D. & Williams, E. S, 1981. Comparison between emission and transmission computed tomography of the liver. *British Medical Journal, 283,* 1212–1214.

Laird, E. E., Rajathurai, A, Williams, E.D., Mittra, B. & Rankin, D., 1984. Quantitative analysis of rotating gamma camera thallium-201 scintigrams of myocardium. *Nuclear Medicine Communications, 5,* 577–586.

Lang, P, Gerlock, A. J. & Rusu, J., 1979. Arteriography: aid to urography in determining etiology and diagnosis of renal pseudotumours. *American Journal of Roentgenology, 133,* 149–151.

Larsson, S. A., 1980. Gamma camera emission tomography *Acta Radiologica Supplementum, 363.*

Mahoney, B. S, Jeffrey, R B. & Laing, F. C., 1983. Septa of Bertin: a sonographic pseudotumour. *Journal of Clinical Ultrasound, 11,* 317–319.

Maisey, M., 1980. *Nuclear Medicine A Clinical Introduction* (Update Books, London), p. 70.

Metz, C. E., 1978. Basic principles of ROC analysis. *Seminars in Nuclear Medicine, 8,* 283–298.

O'Reilly, P. H., Shields, R. A & Testa, H. J., 1979. *Nuclear Medicine in Urology and Nephrology* (Butterworths, London), p. 152.

O'Reilly, P H., Osborn, D. E., Testa, H. J., Asbury, D. L, Best, J J. K & Barnard, R. J., 1981. Renal imaging: a comparison of radionuclide, ultrasound, and computed tomographic scanning in investigation of renal space-occupying lesions. *British Medical Journal, 282,* 943–945

Shea, G., 1978 An analysis of the Bayes' procedure for diagnosing multistage diseases. *Computers and Biomedical Research, 11,* 65–75

Sherwood, T., 1975 Renal masses and ultrasound. *British Medical Journal, iv,* 682–683.

Starr, S. J, Metz, C. E., Lusted, L B. & Goodenough, D. J., 1975. Visual detection and localization of radiographic images. *Radiology, 116,* 533–538.

Swets, J. A. & Pickett, R. M., 1982. *Evaluation of Diagnostic Systems* (Academic Press, New York).

Tamaki, N., Yonekura, Y., Mukai, T., Fujita, T., Nohara, R., Kadota, K., Kambara, H., Kawai, C., Torizuka, K & Ishii, Y., 1984. Segmental analysis of stress thallium myocardial emission tomography for localisation of coronary artery disease *European Journal of Nuclear Medicine, 9,* 99–105

Thornbury, J. R, McCormick, T. L. & Silver, T. M., 1980. Anatomic/radiologic classification of renal cortical nodules. *American Journal of Roentgenology, 134,* 1–7

Williams, E D. & Parker, C., 1982. Kidney pseudotumour diagnosed by emission computed tomography, *British Medical Journal, 285,* 1379–1380

Williams, E D, Parker, C., Roy, R. R., Rankin, D., Holland, A. & Brown, M., 1982 Multiple section emission computed tomography of the kidney: an assessment. In *Radionuclides in Nephrology* Ed. by A M. Joekes, A. R. Constable, N. J. G. Brown & W. N Tauxe (Academic Press, London), pp 71–75.

Williams, E. D., 1983. Evaluation of clinical image processing and presentation in gamma camera emission tomography (abstract) *Clinical Physics and Physiological Measurement, 4,* 96.

Williams, E. D., Rankin, D., Laird, E. E., Brown, M. A., Blair, R & Ennew, Y, 1983 Image presentation in emission tomography (abstract). *Nuclear Medicine Communications, 4,* 168.

Williams, E.D., Parker, C., Roy, R. R. & Rankin, D., 1984 Clinical evaluation of rotating gamma camera tomography of the kidney (abstract). *British Journal of Radiology, 57,* 947.

Book review

Manual of Darkroom Technique. WHO Basic Radiological System. By P. E. S. Palmer, pp. 16, 1985 (World Health Organization, Geneva), Sw. fr. 8.
ISBN 92-4-154178-4

A great deal of work and thought have been put into designing equipment for the BRS system, but another very important factor in the achievement of successful radiographs has, until now, been neglected in the literature from the World Health Organization. The *Manual of Darkroom Technique* forms part of a programme to promote simple, safe and economic diagnostic radiology appropriate for use in rural or isolated hospitals or clinics.

It consists of a comprehensive set of instructions and explanations written with the aim of producing well processed radiographs in places where there is little or no expert supervision. The author rightly states that, in terms of patient care, a poor-quality radiograph is more harmful than if the patient has no radiographic examination at all.

The text is written in clear, simple language which people with little or no prior knowledge of darkroom technique will find easy to understand. The simplicity of wording has the added advantage that it can be translated easily for use in countries where the BRS system will be operating.

The manual consists partly of a simple text, which should be read before the second part of the manual which consists of illustrated instructions Together, the two parts give a step-by-step explanation of the method of processing films, the making up and maintenance of processing chemicals, and a few "dos and don'ts" of darkroom practice. The book is very short, just 16 foolscap-size pages, and inevitably the coverage of many aspects is brief. Nearly two pages are devoted to record keeping and filing which, although very important, are not really relevant to a manual on darkroom technique.

A very simple layout for a darkroom is shown, indicating that there should be a drywork bench and a separate area for developer and fixer. A rather ambitious item included in this plan is a light "maze". In the simple X-ray department, which is likely for this type of work, a light-proof door (actually mentioned in the text) would appear more sensible. No hint is given in the plan as to where light sockets, safe lights, water or drains would be most suitably sited. Mention is made of disposing of old developer and fixer down the "special drain" in the darkroom. This requirement is not mentioned before, nor does it appear on the plan. The necessity for using clean water for rinsing and for washing the films is described. This very valuable point, essential even when water is not freely available, is often given scant attention, with the result that instances have been known where the water was changed at the same intervals as the chemicals. Mention is made that the chemicals in the tanks should be replenished "as necessary", but it would be more helpful to state that the levels must always be high enough to cover the film being processed to avoid essential information on the radiograph being excluded. In the instructions on cleaning intensifying screens, it should have been stressed that the cleaning cloths should be only slightly damp to avoid excessive wetting of the screens.

These are minor criticisms of a manual which achieves its aim of being an easily understood basic manual of darkroom processing. Inevitably, those experienced in teaching darkroom techniques will find they would have stressed certain aspects, or treated them differently, but this does not detract from the value of this publication. Excellent books on processing have been produced by major manufacturers of X-ray film for many years. However, these are usually written for workers in established hospitals or clinics where the techniques of radiographic processing are known already. The need has existed for a really simple manual, easily understood by those for whom practical help is not readily available. Professor Palmer has made a timely contribution to assist those working in isolated or rural clinics and forming part of the World Health Organization's Basic Radiological System

GLENDA J. BRYAN

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Ultrasonic visualisation of the inflamed appendix

By S. Karstrup, M.D., S. Torp-Pedersen, M.D. and *O. Roikjaer, M.D.

Department of Ultrasound and *Department of Surgical Gastroenterology, University Hospital, Herlev, Denmark

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ABSTRACT

A prospective ultrasonic study of the right lower abdominal quadrant was performed in 46 patients prior to appendicectomy. Ultrasonography revealed an inflamed appendix in 24 out of 29 patients with appendicitis and excluded its presence in 16 out of 17 patients without appendicitis. The ultrasonic pattern of the inflamed appendices appeared as echo-poor/echo-free lesions with lack of movement. In six of seven patients with perforated appendices, ultrasonography revealed free intra-abdominal fluid in addition to bowel disease. The possible value of abdominal ultrasound in patients with suspected acute appendicitis is discussed.

Characteristic sonographic patterns of both normal and abnormal segments of bowel have been described, allowing the recognition of an increasing number of pathological lesions (Fleischer et al, 1980). The findings and value of ultrasonic examination of the inflamed appendix have been described in only a few selective cases (Deutsch & Leopold, 1981; Preusser, 1981; Parulekar, 1983; Claes et al, 1984). We report a larger series of patients ultrasonically examined prior to appendicectomy.

METHODS

Forty-six patients (24 men and 22 women) were examined immediately before surgery for acute appendicitis; the median age was 32 (range 16–80) years. For practical reasons, since most appendicectomies were performed in the evening or at night, the random choice of patients for the study was based on days where all patients could be examined preoperatively in a 24 h period, from 8 a.m. to 8 a.m.

The ultrasonic examination was deliberately restricted to the right lower abdominal quadrant in order to avoid abnormalities of other abdominal regions influencing the diagnosis of appendicitis. Only two ultrasonic conclusions were possible: inflamed appendix seen or inflamed appendix not seen. The result of ultrasonography was not made known to the surgeon. The ultrasound diagnosis was compared with the operative findings and with the pathology report.

The examinations were carried out using a 5 MHz curved array scanner (Picker LSC 7000) and the study was in accordance with the principles of the Helsinki declaration.

RESULTS

Accuracy

Based on histological examination of the removed appendices, 29 of the 46 patients (63%) had acute appendicitis. Ultrasonic examination revealed an inflamed appendix in 24 of the 29 (83%; 95% confidence limits, 64–94%) and excluded the presence of an inflamed appendix in 16 of the 17 patients without acute appendicitis (94%; 95% confidence limits, 71–100%) (Table I).

Of the five patients with inflamed appendices not seen by ultrasonography, two examinations were inconclusive because gas-filled bowel loops prevented sonographic evaluation. In the remaining three patients, two had suppurative appendicitis and one had inflammation limited to the superficial mucosal layers. The single false positive finding was caused by leakage into the right lower abdominal quadrant from a ruptured aortic aneurysm. Seven patients had perforated appendices. In six of these, ultrasonography disclosed free intra-abdominal fluid in addition to diseased bowel.

The normal appendix could not be visualised.

Sonographic features

The sonographic pattern of the inflamed appendix appeared as an echo-poor/echo-free lesion with a rounded, ovoid or curved configuration, probably depending on the site of the appendix (Fig. 1). In only two cases was it possible to visualise the long axis of the inflamed appendix in one plane (Fig. 1). Although peristaltic movements were seen in the surrounding bowel loops, the lesion itself was immobile without demonstrable movements or change in configuration.

Gas-filled bowel loops producing a pattern of diffuse echoes were seen in almost every patient. Nevertheless, in almost every case it was possible to obtain acceptable images, as peristalsis caused movement of the gas which could be displaced by pressure of the transducer.

TABLE I

ULTRASONIC AND HISTOLOGICAL DIAGNOSIS IN 46 PATIENTS WITH SUSPECTED INFLAMED APPENDICES

Histology	Ultrasound	
	Positive	Negative
Positive	24	5
Negative	1	16

PV_{pos}: 24/25 × 100% = 96% (95% confidence limits, 78–100%).

PV_{neg}: 16/21 × 100% = 76% (95% confidence limits, 53–92%).

Author for correspondence: Steen Karstrup, M.D., Department of Ultrasound, Herlev Hospital, University of Copenhagen, DK-2730 Herlev, Denmark.

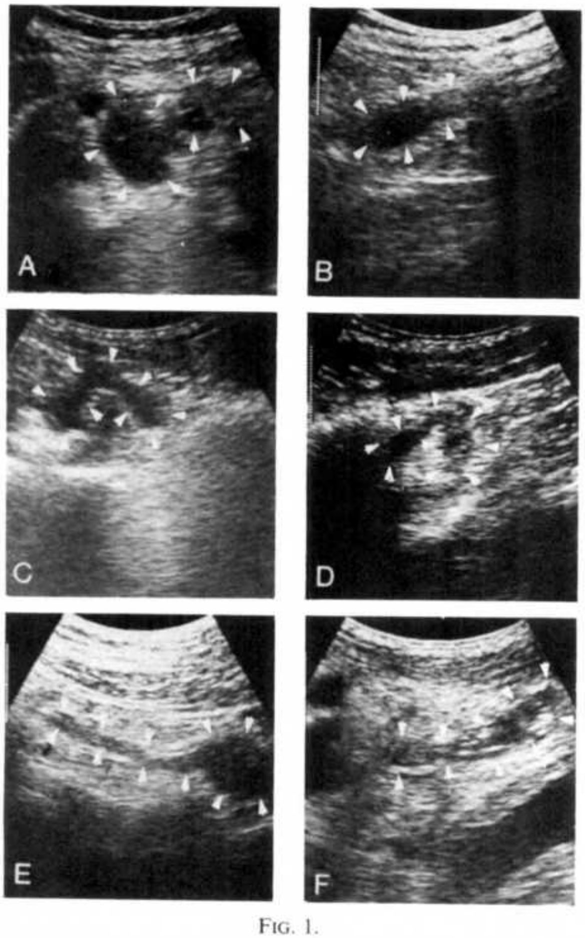

FIG. 1.

The echographic patterns and different configurations of inflamed appendices in six patients. (A) and (B) show round or ovoid lesions. (C) and (D) show curved or crescentic lesions; at operation the appendix in (D) was found to be retrocaecal and curved towards the ileocaecal junction. Scans (E) and (F) were from the only cases where the inflamed appendices could be visualised in their long axis in one plane; in (E) the inflammatory process was predominantly in the tip of the appendix.

However, in two patients examination proved impossible because of extreme gaseous distension of the bowel. Both of these patients had a distended abdomen with meteorism.

DISCUSSION

Sonographic characteristics of many types of bowel lesions have been reported (Fleischer et al, 1980; Morgan et al, 1980). Most frequently, abnormal segments demonstrate a target pattern characterised by an anechoic halo wider than 1 cm, representing thickening of the bowel wall, with a central hyperechoic core representing the mucous lining of the bowel lumen and its contents. Bowel segments tend to lack demonstrable movement or change of configuration during peristalsis and show a grossly irregular contour (Fleischer et al, 1980).

In the present study the sonographic pattern of the inflamed appendices appeared as sonolucent lesions. The fact that a central echogenic core was not demonstrated could be explained by the small size of the appendix, by purulent exudate filling the lumen, and by oedema of the mucosa causing the central areas of the lesion to appear echo-poor.

This study illustrates the possibility of visualising the inflamed appendix. Nevertheless, non-visualisation of an echo-poor/echo-free lesion does not exclude the presence of an inflamed appendix. Acute appendicitis, therefore, continues to remain a difficult diagnosis, particularly in the very young and elderly (Jess, 1983). Furthermore, it may simulate almost any other acute abdominal disease and in turn be mimicked by a variety of gastrointestinal, gynaecological or urological conditions (Jess et al, 1981) in many of which ultrasound has proved to be of benefit (Holm et al, 1980; Braun et al, 1984). The value of abdominal ultrasound as an initial screening procedure in patients suspected of having acute appendicitis or in patients with atypical abdominal symptoms requires further evaluation.

SUPPLEMENT

After the completion of the present manuscript a similar study was reported by Puylaert (1986).

REFERENCES

BRAUN, U., STELLAMOR, K. & LEITNER, H., 1984. Sonographie in der akutdiagnostik des abdomens. *Ultraschall*, *5*, 160–163.

CLAES, H., REYGAERTS, D., LEEMANS, J., DE BOECH, M. & POTVLIEGE, R., 1984. Ultrasonic visualization of the acute inflamed retrocaecal appendix. A report of 4 cases. *Journal Belge de Radiologie*, *67*, 333–336.

DEUTSCH, A. & LEOPOLD, R. G., 1981. Ultrasonic demonstration of the inflamed appendix. *Radiology*, *140*, 163–163.

FLEISCHER, C. A., MUHLETALER, A. C. & JAMES, A. E., 1980. Sonographic patterns arising from normal and abnormal bowel. *Radiologic Clinics of North America*, *18*, 145–159.

HOLM, H. H., KRISTENSEN, J. K., NOERBY RASMUSSEN, S., FOG PEDERSEN, J., HANCKE, S., JENSEN, F., GAMMELGAARD, J. & SMITH, H. E., 1980. *Abdominal Ultrasound. Static and Dynamic Scanning*, 2nd edit. (Munksgaard, Copenhagen).

JESS, P., 1983. Acute appendicitis: epidemiology, diagnostic accuracy, and complications. *Scandinavian Journal of Gastroenterology*, *18*, 161–163.

JESS, P., BJERREGAARD, B., BRYNITZ, S., HOLST-CHRISTENSEN, J., KALAJA, E. & LUND-KRISTENSEN, J., 1981. Acute appendicitis. *American Journal of Surgery*, *141*, 232–234.

MORGAN, L. C., TROUGHT, S. W., ODDSON, A. T., CLARK, M. W. & RICE, P. R., 1980. Ultrasound patterns of disorders affecting the gastrointestinal tract. *Radiology*, *135*, 129–135.

PARULEKAR, G. S., 1983. Ultrasonic findings in diseases of the appendix. *Journal of Ultrasound in Medicine*, *2*, 59–64.

PREUSSER, R., 1981. Ultrasonographische diagnose einer akuten, phlegmonösen appendizitis. *Wiener Klinische Wochenschrift*, *18*, 587–588.

PUYLAERT, J. B. C. M., 1986. Acute appendicitis: ultrasonic evaluation using graded compression. *Radiology*, *158*, 355–360.

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The non-ionic dimers: a new class of contrast agents

By Peter Dawson and *Michael Howell
Department of Diagnostic Radiology, Hammersmith Hospital, Du Cane Road, London W12 0HS and
*Department of Chemical Pathology, The Middlesex Hospital, Mortimer Street, London W1

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ABSTRACT

Non-ionic dimers are a new class of iodinated radiological contrast agents. Some physico-chemical and pharmacological properties of three representative compounds are presented. Non-ionic dimers are iso-osmolar with plasma at all iodine concentrations unless diluted with saline and in terms of chemotoxicity they appear to be closely comparable with the established non-ionic monomeric agents. It is shown that the data lend support to the theory that it is the degree of steric hindrance of the hydrophobic iodine atoms by side-chains which determines this chemotoxicity. Areas in which agents of this type may find applications are indicated.

Development of the new generation of "low-osmolality" contrast agents has taken two different routes. The first, based on the original idea of Almen (1969), led to the non-ionic tri-iodinated monomeric group of compounds, firstly metrizamide (Amipaque, Nycomed) and, more recently, iohexol (Omnipaque, Nycomed) and iopamidol (Niopam, Bracco). The second led to the ionic hexaiodinated monoacid dimer, ioxaglic acid (Hexabrix, May and Baker). The structures of iohexol and meglumine/sodium ioxaglate (Hexabrix) are illustrated in Fig. 1, with the conventional sodium iothalamate (Conray, May & Baker) for comparison.

Both types of compound have a 3 : 1 ratio of iodine atoms (contrast) to particles in solution (osmolality). This represents a twofold improvement over the 3 : 2 ratio of the conventional compounds.

Aggregation of particles in solution results in a higher effective molecular weight and a somewhat greater reduction in osmolality than the 50% suggested by these numbers (Dawson et al, 1983).

At the high iodine concentrations favoured by radiologists for some applications (300–400 mg/ml iodine) the 3 : 1 ratio compounds still have osmolalities approximately two to three times that of plasma. An obvious next developmental step would be to combine the two approaches and to synthesise a non-ionic hexaiodinated dimer. Such a compound would have an iodine-to-particle ratio of 6 : 1, giving a further theoretical halving of the osmolality at any given iodine concentration. Thus, solutions with iodine concentrations in the 300–400 mg/ml iodine range would be expected to be very close in osmolality to that of plasma. This attractive idea has been pursued by several pharmaceutical companies who have synthesised experimental compounds, three of which are illustrated in Fig. 2.

In so far as the toxicity of a contrast agent is partly a function of its degree of hyperosmolality, such compounds would appear to promise an improvement even over the excellent 3 : 1 ratio non-ionic monomeric and monoacid dimeric agents. Systemic toxicity is not, however, a function only of osmolality, but depends also on chemical structure (chemotoxicity). Indeed, since these 3 : 1 ratio agents completely eliminate the osmolality problem, their clinical toxicity will be dictated by their chemotoxicity (and any hypersensitivity) which therefore assumes great importance. In this paper a study of the chemotoxicity of the dimers is described with some data on their chemistry and physical properties.

CHEMISTRY AND PHYSICAL PROPERTIES

The contrast agents used in this study are listed in Table I and their structures are illustrated in Figs 1 and 2.

Osmolality

The osmolalities, as a function of iodine concentration, are shown in Fig. 3. All three dimers studied are so close in osmolality that, to maintain clarity, only one curve has been plotted to represent them. It will be seen that the dimer osmolality is actually *less* than that of plasma until iodine concentrations greater than 400 mg/ml are reached. This is the result of aggregation of molecules leading to a greater effective molecular weight and a reduced osmolality. Since *hypo*-osmolality might be considered undesirable, the manufacturers add small amounts of saline to the finished product so that their osmolality is raised to that of plasma.

Viscosity

Figure 4 illustrates the viscosities of the dimeric agents, with iohexol for comparison, as a function of iodine concentration, at 20°C and 37°C. Again, all three dimers are closely similar, so only one curve is illustrated. It is immediately apparent that viscosity, as might be predicted with such large molecules, is higher than that of the monomer. If the temperature is raised to 37°C, for which a sensible case can in any event be made, the viscosity falls to a level below that of iohexol at 20°C. Agents of this type would, therefore, be quite usable in angiography if other properties were acceptable.

In myelography higher viscosity may be regarded as a positive asset as it mitigates against rapid diffusion and

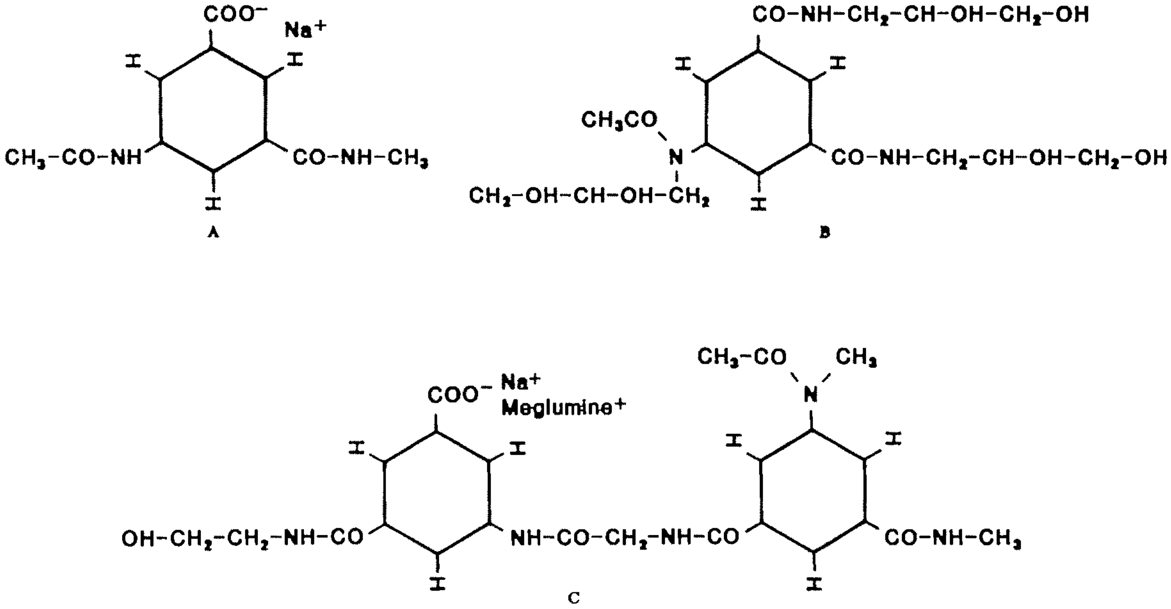

FIG. 1.
The structures of (A) sodium iothalamate, (B) iohexol and (C) meglumine/sodium ioxaglate.

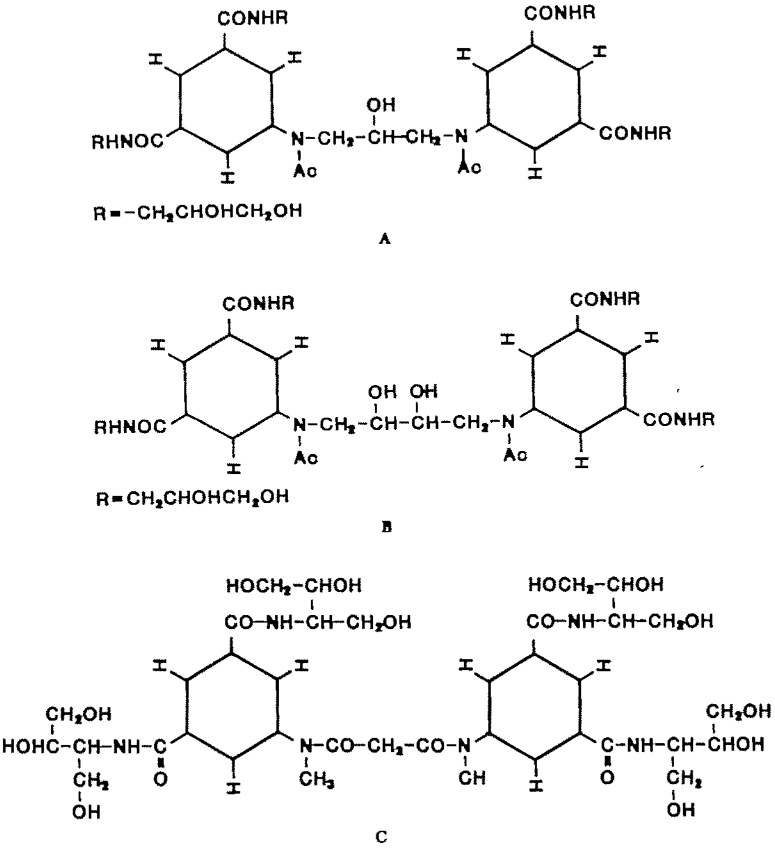

FIG. 2.
The structure of the non-ionic dimers studied: (A) iodixanol (Compound 2-5410-3A, Nycomed), Compound 2-5410-4A (Nycomed) and (C) iotrolan (Compound ZK39.482, Schering AG).

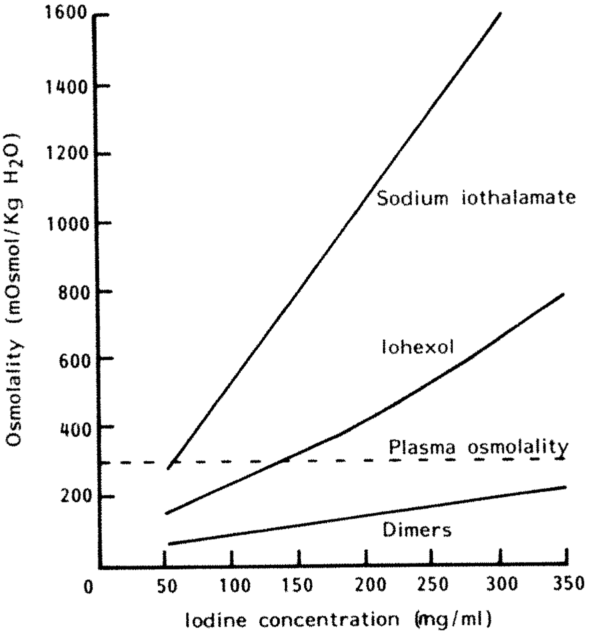

FIG. 3.

Osmolalities as a function of iodine concentration at 37°C (data from May and Baker, Nycomed and Schering AG).

dilution in the cerebrospinal fluid and against rapid diffusion out of the spinal theca.

TOXICITY OF CONTRAST AGENTS

The toxicity of iodinated contrast agents is a function of osmolality, electric charge, chemotoxicity and hypersensitivity.

Conventional contrast agents are toxic because of their high osmolality (up to 7.5 times that of plasma). Non-ionic monomeric agents and the monoacid dimeric agent, though called "low-osmolality" agents, still have osmolalities two to three times that of plasma at higher iodine concentrations and still possess some toxicity on this basis. The non-ionic dimers, however, can be made iso-osmolar with plasma at all concentrations (with added saline if necessary) and possess no such toxicity.

Ionic agents possess a toxicity as a consequence of their electric charge. This is certainly important in neurotoxicity in myelography, but its importance in general systemic toxicity has probably been exaggerated. The non-ionic dimers possess no electric charge and hence no charge-based toxicity. Any toxicity manifested by the non-ionic dimers will derive from their chemical structure.

Many phenomena have been studied to assess chemotoxicity (Dawson & Edgerton, 1983). The one on which particular interest has been focused is enzyme inhibition. Inhibition of the enzyme acetylcholinesterase, in particular, has not only proved a good indicator for clinical toxicity with a large number of contrast agents, but may also be the basic mechanism of some contrast agent side-effects. It was therefore used to assess the chemotoxicity of the non-ionic dimers. The techniques have been described in detail elsewhere (Howell & Dawson, 1985).

TABLE I

CONTRAST AGENTS USED IN THE STUDY

Proprietary name	Non-proprietary name	Manufacturer
Conray 420	sodium iothalamate	May and Baker
Omnipaque	iohexol	Nycomed
Compound 2-5410-3A	iodixanol	Nycomed
Compound 2-5410-4A	(as yet unnamed)	Nycomed
Compound ZK39.482	iotrolan	Schering AG

RESULTS

Figure 5 shows the percentage of acetylcholinesterase activity remaining plotted against the iodine concentration of the contrast media (mg/ml) in the reaction mixture. All points plotted are the mean of 10 analyses at that iodine concentration. There is an approximately straight-line relationship between inhibition of acetylcholinesterase activity and iodine concentration for each agent. The conventional ionic agents (represented by sodium iothalamate) form a group having a larger effect on the enzyme and the non-ionic monomeric

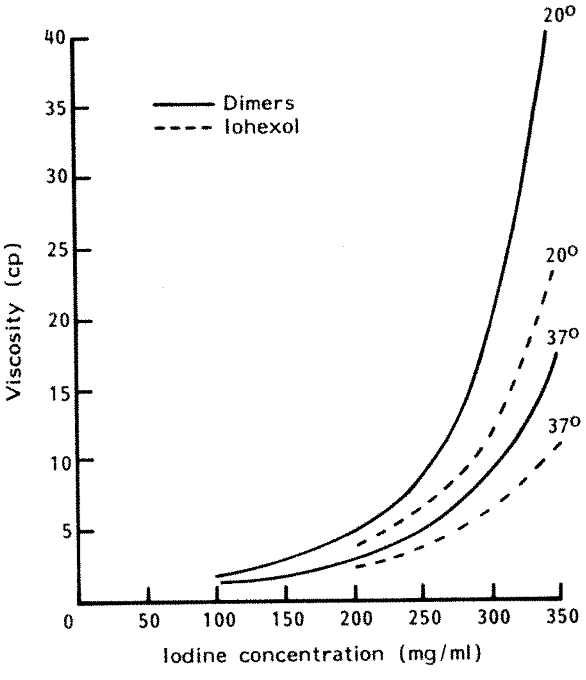

FIG. 4.

Viscosities at 37°C and 20°C as a function of iodine concentration (data from Nycomed and Schering AG).

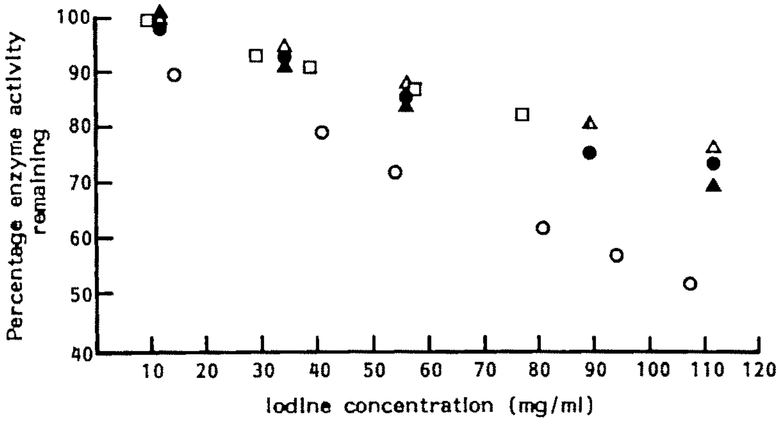

FIG 5

Enzyme inhibition by contrast agents as a function of iodine concentration. Each point is the mean of 10 assays: ○ iothalamate, ● iohexol, ▲ iodixanol, △ Compound 2-5410-4A, □ iotrolan.

agents form another group having a lesser effect, as previously described (Dawson & Edgerton, 1983). Interestingly, the non-ionic dimeric agents seem, properly, to belong in the latter group, all having a very similar effect to that of the non-ionic monomers.

A Lineweaver-Burk plot (Conn & Stumpf, 1972; Howell & Dawson, 1985) of the enzyme inhibition data, not shown, confirmed that the inhibition is of a simple competitive character.

DISCUSSION

Contrast agent toxicity has been found to correlate well both with protein binding (Dawson & Edgerton, 1983) and with lipophilicity : hydrophilicity ratio (partition coefficient) (Speck et al, 1983).

The non-ionic dimers have low protein-binding capacity and are highly hydrophilic, suggesting they will have low toxicity. That said, the basic mechanisms of toxicity remain unclear. It may be that inhibition of enzymes by contrast agents binding to them is a fundamental factor. On this model, the low protein-binding capacity and consequent low enzyme inhibitory capacity of the newer agents leads directly to the low toxicity.

As regards lipophilicity · hydrophilicity ratio, iodine groups themselves are highly hydrophobic and on this basis are best shielded (steric hindrance) by hydrophilic groups (Sovak, 1984). This is something poorly achieved in the conventional agents with their short side-chains, but well achieved in both the monomeric and the dimeric non-ionic agents. These compounds, having lost the carboxyl group (which confers such high solubility on the ionic agents), are synthesised with larger side-chains carrying many hydroxyl groups, which give solubility and increase the agents' hydrophilicity, both because the hydroxyl groups are themselves hydrophilic and because they shield the hydrophobic iodine atoms (Howell & Dawson, 1985).

To state these ideas is to say nothing about fundamental mechanisms. It has been suggested recently (Howell & Dawson, 1985) that the iodine groups may be directly responsible for the enzyme inhibitory effect and other aspects of chemotoxicity. This hypothesis would fit the known facts well, but further work needs to be carried out to test it. Such ideas are important because they may allow a prediction of pharmacology from chemical structure.

Whatever the fundamental mechanisms involved, non-ionic dimers satisfy well established criteria for low clinical toxicity. Human studies have not yet been performed, but animal experiments have shown that lethal dose 50% (LD_{50}) levels, a crude measure of toxicity, are indeed very similar for the non-ionic dimers and monomers.

Clinical uses

The non-ionic dimers may find important application in myelography, where their large molecular size and higher viscosity offer positive advantages, as discussed above, particularly as preliminary studies show that their neurotoxicities are very low (Malnor et al, 1984). Their lower osmolalities may offer image-quality improvements in intravenous digital subtraction angiography (DSA) as a result of lesser dilution of the contrast-agent bolus in the central blood volume (Hine et al, 1985).

SUMMARY

The non-ionic dimers are a new group of contrast agents, currently under development. In the useful iodine concentration range they possess osmolalities close to that of plasma. Their viscosities are relatively high, but when warmed to 37° are reduced to acceptable levels for intravascular use. Their chemotoxicities as expressed in enzyme inhibitory capacity are very close to that of iohexol, a non-ionic monomer. This lends support to the theory that it is the degree of steric hindrance of the iodine atoms in contrast agents which dictates their chemotoxicities. It also suggests a low clinical toxicity for the non-ionic dimers comparable with that of the non-ionic monomers. The LD_{50} data

support this prediction. The agents may find particular application in myelography and intravenous DSA.

REFERENCES

ALMEN, T., 1969. Contrast agent design. Some aspects of synthesis of water-soluble contrast agents of low osmolality. *Journal of Theoretical Biology, 24,* 216–226.

CONN, E. E. & STUMPF, P. K., 1972. *Outlines of Biochemistry,* 3rd edit. (John Wiley & Sons Inc., London), p. 171.

DAWSON, P. & EDGERTON, D., 1983. Contrast agents and enzyme inhibition. I. Cholinesterase. *British Journal of Radiology, 56,* 653–656.

DAWSON, P., GRAINGER, R. G. & PITFIELD, J. M., 1983. The new low-osmolar contrast media: a simple guide. *Clinical Radiology, 34,* 221–226.

HINE, A. L., LUI, E. & DAWSON, P., 1985. Contrast agent osmolality and plasma volume changes. *Acta Radiologica Diagnosis, 26,* 753–756.

HOWELL, M. J. & DAWSON, P., 1985. Contrast agents and enzyme inhibition. II. Mechanisms. *British Journal of Radiology, 58,* 845–848.

MALNOR, M., HOUSTON, L. W., TURSKI, P. A., SACKETT, J. F., BOYER, M. & STROTHER, C. M., 1984. Iotrol versus metrizamide in lumbar myelography: a double blind study. Paper delivered to the Radiological Society of North America meeting, Washington, 1984.

SOVAK, M., 1984. Radiocontrast agents. In *Handbook of Experimental Pharmacology.* (Springer-Verlag, Berlin), Vol. 73, p. 1.

SPECK, U., MUTZEL, W. & WEINMANN, H. J., 1983. Chemistry, physiochemistry and pharmacology of known and new contrast media for angiography, urography and CT enhancement. In *Contrast Media in Urography, Angiography and Computerised Tomography.* Ed. by V. Taenzer & E. Zeitler (Georg Thieme Verlag, Stuttgart), p. 2.

Book review

Cerebral Blood Flow and Metabolism Measurement. Ed. by A. Hartmann and S. Hayer, pp. 618, 1985 (Springer-Verlag, Berlin), DM 188.
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This book is the published proceedings of an international symposium on cerebral blood flow (CBF) held in Heidelberg in 1983, but there is a wealth of basic information here, most of which stands the test of time even in a field that is rapidly developing

The start of the book contains a highly relevant and important critique of the xenon washout technique. Most notable is a study of the assumptions of the compartmental analysis of inert gas washout using direct measurement of H_2 diffusion with hydrogen electrodes in the cat brain. They could not confirm the basic assumptions that the tissue is homogeneous and contains no concentration gradients of the tracer, that the arterial tracer concentration is known in the area observed, or that the tumour is removed only by blood from the site sensed.

Compartmental slippage is discussed by Herholz et al. This euphemism for failure of a basic assumption of compartmental analysis was demonstrated to occur with xenon washout and they concluded that the "reliability of regional CBF values obtained by the non-invasive biocompartmental xenon 133 clearance method may vary considerably from region to region". Seylaz and Meric consider the effects of non-instantaneous arrival of tracer in the brain and the contamination due to extracerebral tissues after intravenous injection of xenon. They found the technique reproducible but noted that corrections for Pa CO_2 differences are not appropriate for use in cases of cerebrovascular disorder. O'Brien concludes that the techniques give very good results in normal subjects but errors increase exponentially in pathological states.

A wealth of clinical investigations using xenon washout techniques are recorded: in cerebral ischaemia, stroke, extra-intracranial by-pass surgery, and particularly subarachnoid haemorrhage. Gundling et al summarise the findings as follows: an increase of CBF occurs with rising CO_2 and rising pO_2 and a decrease of CBF occurs with rising pH, haemoglobin and age. Raising blood pressure causes an increase of CBF in subarachnoid haemorrhage but decreasing blood pressure improves CBF in patients with ischaemic stroke. Cerebral blood flow tomography using xenon 133 inhalation is described by Lassen. Paulsen et al show that tissue flow values cannot be obtained from ischaemic areas because of Compton scattering effects Examples of applications in Parkinsonism, mental disorder, stroke and by-pass surgery are given.

These techniques, however, are being overtaken by the use of the new grey-matter imaging agents. First ^{123}I isopropyl-amphetamine, IAMP, and ^{123}I trimethyl-propane-diamine, HIPDM, and more recently ^{99}Tc^{m} HMPAO (although this development post dates this Congress). Raynaud et al compare IAMP and HIPDM in a variety of cerebral disorders. Several authors describe studies of qualitative regional cerebral flow but quantitative estimates remain unobtainable because of incomplete first-pass extraction, efflux from brain tissue and labelled metabolites in the blood.

Quantitative measurement of intracerebral blood flow distribution using a non-diffusible indicator, ^{99}Tc^{m} albumin, in cerebrovascular disease and dementia is described by Nimmon et al.

The stable xenon X-ray CT method for the measurement of CBF is described by Meyer and by Dwyer and Albright and applications are given by other authors. However, the dangers of stable xenon, a respiratory-centre depressant and anaesthetic agent, are stressed by Winkler et al.

The contribution of positron emission tomography (PET) is covered in a major way both in cerebral physiology and clinical applications. The complexities of modelling the metabolism of ^{18}F deoxyglucose by the brain are well described, as are its applications in sensory localisation and cerebrovascular disease. The Hammersmith Group describe ^{15}O as $C^{15}O_2$ for flow, ^{15}O for oxygen uptake and the division of the two for oxygen extraction rates Several authors demonstrate its applications, including Parkinsonism and in cerebral tumour. The curious formulation of cerebral blood flow divided by cerebral blood volume is described by Gibbs et al, apparently not appreciating that this is just the reciprocal of the cerebral mean transit time. The importance of PET in studying ligand interaction with special receptors is only represented by Baron et al describing the use of ^{11}C Ketanserin for investigating 5-hydroxy-serotonin receptors. The volume is completed by some studies of nuclear magnetic resonance (NMR) and ultrasonic procedures Alavi et al present correlative studies of NMR with PET and X-ray CT. Muller et al give a detailed study of the limitations and clinical use of carotid blood flow estimation by Doppler techniques.

In conclusion, there is an enormous amount of detailed, often critically appraised information about the investigation of the brain in health and disease and it is a rewarding book to read or to sample.

KEITH BRITTON

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The influence of a background correction that considers the heart volume on radionuclide left ventricular ejection fraction determination

By *H. Kelbæk, M.D., T. Gjørup, M.D., O. J. Hartling, M.D. and E. Hjortsø, M.D.

Department of Clinical Physiology and Nuclear Medicine, Herlev Hospital, University of Copenhagen, DK-2730 Herlev, Denmark

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ABSTRACT

A correction of background activity that considers the heart volume is introduced in radionuclide equilibrium cardiography. Left ventricular ejection fraction (LVEF) was determined in 19 patients with ischaemic heart disease by multigated equilibrium scan with ^{99}Tc^{m}-labelled red blood cells (^{99}Tc^{m}-RBC). Assuming that the majority of background activity in the ventricular and periventricular regions of interest arises from ^{99}Tc^{m}-RBC in lung tissue, a ventricular/periventricular background ratio was calculated from the distribution of ^{99}Tc^{m}-labelled macroaggregated albumin. The mean relative distribution of pulmonary ^{99}Tc^{m}-RBC activity in the ventricular region of interest was 0.590 (range 0.279–1.061) compared with the periventricular region. The modified background correction resulted in a mean LVEF of 43.0% (range 12.9–67.6%) compared with 46.8% (range 10.9–67.8%) with the standard correction, $p < 0.005$. Since no attempt was made to calculate the proportion of ^{99}Tc^{m}-RBC activity arising from the myocardium and thoracic wall, this difference represents an upper limit of the general overestimation of LVEF obtained by the standard calculation. A further decrease in LVEF was seen when no background correction was applied. The present results suggest that standard LVEF calculation, by neglecting the background volume displaced by the cardiac blood pool, results in a slight overestimation of LVEF.

Some investigators have assessed radionuclide left ventricular ejection fraction (LVEF) without correction for background radioactivity in the ventricular region of interest (Luig et al, 1979; Karsch et al, 1980). Others have stressed the importance of background correction in the determination of LVEF and left ventricular volumes by the equilibrium method (Williams & Hamilton, 1978; Taylor et al, 1980; Reiber et al, 1983; Seiderer et al, 1983). The standard background evaluation utilises either peridiastolic or perisystolic radioactivity to adjust for activity lying in front of and behind the heart with normalisation of the periventricular area for ventricular size (Parker et al, 1972; Green et al, 1978; Slutsky et al, 1979; Bar-Shlomo et al, 1982; Froelich et al, 1983). However, the standard calculation of LVEF does not consider the "displacement" of background by the actual ventricular volumes, which are thereby underestimated.

In the present study we took the first step to estimate the influence of this phenomenon by measuring the radioactivity of ^{99}Tc^{m}-labelled red blood cells (^{99}Tc^{m}-RBC) located in the pulmonary tissue in front of and behind the heart in proportion to the ^{99}Tc^{m}-RBC activity in the periventricular lung region.

MATERIAL AND METHODS

Theoretical considerations

Left ventricular ejection fraction, determined by the standard method, was calculated by the formula:

$$\mathrm{LVEF} = \frac{\mathrm{EDA(EDC-BGC)-ESA(ESC-BGC)}}{\mathrm{EDA(EDC-BGC)}} = 1-\frac{\mathrm{ESA(ESC-BGC)}}{\mathrm{EDA(EDC-BGC)}} \qquad (1)$$

where EDA = end-diastolic area (pixels), EDC = activity in EDA (counts per pixel), BGC = background (periventricular) counts per pixel, ESA = end-systolic area, and ESC = activity in ESA (counts per pixel).

It was assumed that the relation between the ^{99}Tc^{m}-RBC activity in front of and behind the left ventricle ("true"-BG) and the ^{99}Tc^{m}-RBC activity in the periventricular region (BGC) could be presented by the relation between the pulmonary blood flows in the respective regions (Fig. 1). It was also assumed that the pulmonary blood flows could be presented by the distribution of ^{99}Tc^{m}-labelled macroaggregated albumin (^{99}Tc^{m}-MAA) trapped in the lung capillaries after intravenous injection and located in the end-diastolic (MAA-EDC), end-systolic (MAA-ESC) and periventricular background regions (MAA-BGC). Thus,

$$\frac{\text{“true”-BG in end-diastole}}{\mathrm{BGC}} = \frac{\mathrm{MAA\text{-}EDC}}{\mathrm{MAA\text{-}BGC}}$$

and

$$\frac{\text{“true”-BG in end-systole}}{\mathrm{BGC}} = \frac{\mathrm{MAA\text{-}ESC}}{\mathrm{MAA\text{-}BGC}} \qquad (2)$$

A modification of Equation (1) with the aid of Equation

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*Author for correspondence.

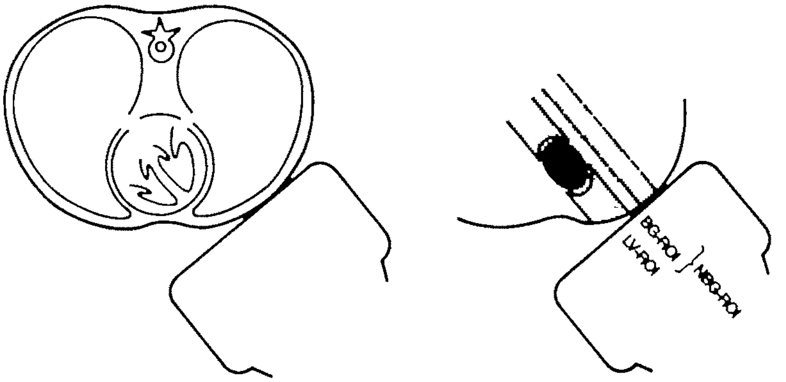

FIG. 1.
The true background activity is located in front of and behind the left ventricle (dark area) in the left ventricular region of interest (LV-ROI). The standard background activity is calculated in a background region of interest (BG-ROI) in the periventricular region. This area is normalised for ventricular size (NBG-ROI). It is seen that the normalised area overestimates the true background activity because it does not consider the ventricular volume

(2) results in the modified LVEF calculation:

$$\text{LVEF} = 1 - \frac{\text{ESA}(\text{ESC} - \text{BGC} \times (\text{MAA-ESC}/\text{MAA-BGC}))}{\text{EDA}(\text{EDC} - \text{BGC} \times (\text{MAA-EDC}/\text{MAA-BGC}))} \quad (3)$$

Left ventricular ejection fraction determined without background correction was calculated by:

$$\text{LVEF} = 1 - \frac{\text{ESA} \times \text{ESC}}{\text{EDA} \times \text{EDC}} \quad (4)$$

Study protocol

Thirteen men and six women, aged 42–73 (mean 60) years, with ischaemic heart disease underwent determination of radionuclide LVEF at supine rest. Autologous red blood cells (RBC) were labelled *in vitro* with approximately 925 MBq (25 mCi) $^{99}\text{Tc}^{\text{m}}$ and reinjected. Data were collected by a gamma scintillation camera equipped with a high-sensitivity parallel-hole collimator and a computer system (Scintiview, Siemens). Left ventricular ejection fraction was determined in the left anterior oblique projection with a 5–10° caudal tilt.

Multiple electrocardiographic-gated equilibrium blood scintigrams were achieved by division of each cardiac cycle into 16 frames. Activity was compiled over 600–800 beats. Data were acquired in a 64 × 64 frame format. The left ventricular end-diastolic and end-systolic areas were manually delineated in a 128 × 128 format matrix. The background area was drawn just infero-lateral of the ventricle in the end-diastolic frame and normalised for ventricular size (Fig. 1). The reproducibility of this method has proved acceptable in our laboratory.

Three repeat measurements of LVEF were performed with identical acquisition duration. The *in-vivo* half-life of $^{99}\text{Tc}^{\text{m}}$-RBC was calculated from the two first acquisitions. Immediately before the third LVEF acquisition approximately 148 MBq (4 mCi) of $^{99}\text{Tc}^{\text{m}}$-MAA was administered intravenously. The activity arising from MAA in the third acquisition was calculated using:

$$A_3\,(\text{MAA}) = A_3\,(\text{Total}) - A_3\,(\text{RBC})$$

Values of LVEF obtained by Equations 1, 2 and 3 were compared. Statistical analysis was performed by means of the *t*-test for paired and unpaired data. A p value < 0.05 was considered significant.

RESULTS

The activity ratios of $^{99}\text{Tc}^{\text{m}}$-MAA in the ventricular and periventricular region of interest are recorded in Table I. The MAA ratios EDC/BGC and ESC/BGC ranged from 0.279 to 0.945 (mean 0.591) and 0.289 to 1.061 (mean 0.588). This difference was not significant.

The modified background correction resulted in a mean LVEF of 43.0% (range 12.9–67.7%) compared with 46.8% (range 10.9–67.8%) with the standard background correction; $p < 0.005$ (Table I). No background correction resulted in a further decrease in mean LVEF, to 39.8% (range 9.2–59.5%), $p < 0.001$ compared with the standard background correction.

Comparison of the standard and modified background corrections demonstrated LVEF differences smaller than 5% in 12 patients. In five patients the difference was 5–10%, leaving only two patients with an LVEF difference greater than 10%.

DISCUSSION

Preferences vary concerning the best method of subtracting counts that do not originate from the left ventricle (Ashburn et al, 1978), and various background subtraction regimes have resulted in widely different values of LVEF. Karsch et al (1980) found an excellent correlation between LVEF determined by radionuclide cardiography and contrast cineventriculography despite the fact that LVEF was determined *without* background correction. In contrast, Reiber et al (1983) found that a method using separate end-diastolic and end-systolic contours and a background region showing minimal variance throughout the cardiac cycle correlated best with the contrast ventriculography. This method of background subtraction corresponds to that employed by others (Pfisterer et al, 1979; Wackers et al, 1979) who have tested the validity of the technique. Some authors have recommended that each laboratory using radionuclide methods should develop its own correction by appropriate regression equations to give values of

TABLE I

ACTIVITY OF ^{99}Tc^m-RBC AND ^{99}Tc^m-MAA IN THE LEFT VENTRICULAR AND BACKGROUND REGIONS OF INTEREST

Case	^{99}Tc^m-RBC activity					^{99}Tc^m-MAA activity		LVEF (%)		
	EDC (counts per pixel)	EDA (pixels)	ESC (counts per pixel)	ESA (pixels)	BGC (counts per pixel)	EDC/BGC	ESC/BGC	background correction		no background correction
								standard	modified	
1	70.76	937	59.01	455	26.88	0.279	0.462	64.4	64.2	59.5
2	78.19	1229	75.95	822	27.08	0.870	0.677	36.0	29.4	35.0
3	75.45	1114	61.37	715	38.08	0.516	0.426	60.0	48.0	47.8
4	57.01	748	48.20	392	19.17	0.387	0.289	59.8	54.9	55.7
5	91.17	938	85.46	770	32.92	0.433	0.396	26.0	22.7	23.1
6	81.43	1396	79.41	1148	22.87	0.754	0.696	20.6	18.7	19.8
7	78.01	1256	64.44	774	31.36	0.789	0.735	56.3	52.1	49.1
8	84.05	767	60.13	548	36.17	0.357	0.320	64.2	51.2	48.9
9	85.47	867	73.83	556	30.85	0.336	0.337	49.5	45.2	44.6
10	81.91	829	74.93	630	27.73	0.672	0.897	33.8	39.9	30.5
11	75.87	1207	61.49	798	34.97	0.491	0.583	57.1	53.7	46.4
12	75.53	1674	69.09	596	19.82	0.536	0.634	10.9	12.9	9.2
13	71.30	1025	58.45	844	43.62	0.836	0.830	55.9	47.5	32.5
14	75.70	1435	76.45	1130	28.23	0.416	0.296	20.0	16.2	20.5
15	74.05	1316	57.96	796	33.06	0.945	1.061	63.2	67.6	52.6
16	70.43	1338	54.90	914	26.94	0.525	0.534	56.1	50.8	46.7
17	66.31	893	53.21	475	33.09	0.338	0.331	67.8	59.2	57.3
18	80.74	1057	74.25	871	32.38	0.892	0.833	28.7	24.9	24.2
19	73.19	1098	58.72	638	22.14	0.829	0.842	58.4	57.5	53.4
Mean	76.14	1112	65.64	730	29.86	0.591	0.588	46.8	43.0	39.8
SD	7.55	253	10.24	208	6.32	0.200	0.236	18.1	17.0	15.0

EDC = end-diastolic counts, EDA = end-diastolic area, ESC = end-systolic counts, ESA = end-systolic area, BCG = background counts, ^{99}Tc^m-RBC = ^{99}Tc^m-labelled red blood cells, ^{99}Tc^m-MAA = ^{99}Tc^m-labelled macroaggregated albumin.

radionuclide LVEF that agree with contrast ventriculography based on a series of patients undergoing both investigations (Folland et al, 1977). However, it is noticeable that the cineventriculographic contrast method itself has inherent limitations (Dodge et al, 1966), and that its value as a reference method is therefore limited.

We found that the ratio between the "pulmonary" activity located in front of and behind the left ventricle and that located in the periventricular region varied from 28% to 106% (Table I). This demonstrates wide anatomical differences in patients with ischaemic heart disease and probably reflects variations in both heart size and the ventricular depth in the thoracic cavity (Seiderer et al, 1983). Background activity in other than pulmonary tissue was not regarded because of the lack of appropriate models to calculate these activities. A considerable ^{99}Tc^m-RBC activity in the myocardium and thoracic wall would tend to reduce the difference in activity in the "true" and the periventricular background regions. Thus, the modification factor of the standard background correction should actually be smaller than that applied in the present study. The modified background correction in our study resulted in a mean LVEF reduction by 3.8%, which therefore represents an upper limit of the general overestimation of LVEF by the standard correction.

Left ventricular ejection fraction was reduced in 16 out of 19 patients (84%; 95% confidence limits, 60–97%). The largest absolute differences between the standard and modified LVEF values were found in patients in whom the ratio MAA-EDC/MAA-BGC was larger than the ratio MAA-ESC/MAA-BGC, in patients where these ratios were low and in patients with good ventricular function. Large relative LVEF differences were generally found in patients in whom the MAA ratios differed markedly and in whom the ventricular volumes were large.

It should be noted that the modification of the LVEF calculation applied in this study, cf. Equation 3, assumes that the ratio between ^{99}Tc^m-RBC activity in front of and behind the left ventricle and ^{99}Tc^m-RBC activity in the periventricular region equals the ratio between the pulmonary blood flows in the similar regions. This approach implies that the distribution of major vessels supplying distant tissues is rather uniform in the respective regions. In cases with more major vessels in the periventricular than in the "true" background region, the modification factor would be underestimated. Still, this underestimation would serve to counterbalance the neglected myocardial and thoracic wall radioactivity as mentioned above.

In conclusion, the present study demonstrates various sizes of the pulmonary blood flow located in the left ventricular region of interest in patients with ischaemic heart disease. Left ventricular ejection fraction calculated with a modified background correction that considers the heart volume, compared with a standard correction results in slight reductions of LVEF in most cases. In some patients the LVEF reduction may reach clinical significance.

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REFERENCES

Ashburn, W. L., Schelbert, H. R. & Verba, J. W., 1978. Left ventricular ejection fraction—a review of several radionuclide angiographic approaches using the scintillation camera. *Progress in Cardiovascular Diseases, 20,* 267–284.

Bar-Shlomo, B.-Z., Druck, M. N., Morch, J. E., Jablonsky, G., Hilton, J. D., Feiglin, D. H. I. & McLaughlin, P. R., 1982. Left ventricular function in trained and untrained healthy subjects. *Circulation, 65,* 484–488.

Dodge, H. T., Sandler, H., Baxby, W. A. & Hawly, R. R , 1966. Usefulness and limitations of radiographic methods for determining left ventricular volume. *American Journal of Cardiology, 18,* 10–24.

Folland, E. D., Hamilton, G. W., Larson, S. M., Kennedy, J. W., Williams, D. L. & Ritchie, J. L., 1977. Radionuclide ejection fraction: a comparison of three radionuclide techniques with contrast angiography. *Journal of Nuclear Medicine, 18,* 1159–1166.

Froelich, J. W., Thrall, J. H , Kalff, V., Rogers, W. L. & Rabinovitch, M., 1983. Computer analysis of cardiac radionuclide data. *Progress in Cardiovascular Diseases, 26,* 43–74.

Green, M. V., Brody, W. R., Douglas, M. A., Borer, J. S., Ostrow, H. G., Line, B. R., Bacharach, S. L. & Johnston, G. S., 1978. Ejection fraction by count rate from gated images. *Journal of Nuclear Medicine, 19,* 880–883.

Karsch, K. R., Schicha, H., Rentrop, P., Kreuzer, H. & Emrich, D., 1980. Validity of different gated equilibrium blood pool methods for determination of left ventricular ejection fraction. *European Journal of Nuclear Medicine, 5,* 439–445.

Luig, H., Bartella, R., Carstens, B., Domovitz, S., Reuter, R , Emrich, D., Faccoro, L., Schicha, H., Graf, M., Karsch, K. R., Rentrop, P. & Kreuzer, H., 1979. The determination of the left ventricle volume curve without background correction and its validation by direct intercomparison with the ejection fractions as determined by biplane laevocardiography. *Nuclear Medicine, 18,* 120–124.

Parker, J. A., Secker Walker, R., Hill, R., Siegel, B. A. & Potchen, E. J., 1972. A new technique for the calculation of left ventricular ejection fraction. *Journal of Nuclear Medicine, 13,* 649–651.

Pfisterer, M. E., Ricci, D. R., Schuler, G., Swanson, S. S., Gordon, D. G., Peterson, K. E. & Ashburn, W. L., 1979. Validity of left ventricular ejection fractions measured at rest and peak exercise by equilibrium radionuclide angiography using short acquisition times. *Journal of Nuclear Medicine, 20,* 484–490.

Reiber, J. H. C., Lie, S. P., Simoons, M. L., Hoek, C., Gerbrands, J. J., Wijns, W., Bakker, W. H. & Kooij, P. P. M., 1983. Clinical validation of fully automated computation of ejection fraction from gated equilibrium blood pool scintigrams *Journal of Nuclear Medicine, 24,* 1099–1107.

Seiderer, M., Bohn, I., Buell, U., Kleinhans, E. & Strauer, B. E., 1983. Influence of background and absorption correction on nuclear quantification of left ventricular end diastolic volume. *British Journal of Radiology, 56,* 183–187.

Slutsky, R., Karliner, J., Ricci, D., Kaiser, R., Pfisterer, M., Gordon, D., Peterson, K. & Ashburn, W., 1979. Left ventricular volumes by gated equilibrium radionuclide angiography: a new method. *Circulation, 60,* 556–574.

Taylor, D. N., Garvie, N. W., Harris, D., Sharratt, G. P., Goddard, B. A. & Ackery, D. M., 1980. The effect of various background protocols on the measurement of left ventricular ejection fraction in equilibrium radionuclide angiography. *British Journal of Radiology, 53,* 205–209.

Wackers, F. J. T., Berger, H. J., Johnstone, D. E., Goldman, L., Reduto, L. A., Langou, R. A., Gottschalk, A. & Zaret, B. L., 1979 Multiple gated cardiac blood pool imaging for left ventricular ejection fraction· validation of the technique and assessment of variability. *American Journal of Cardiology, 43,* 1159–1166.

Williams, D. L. & Hamilton, G. W., 1978. The effect of errors in determining left ventricular ejection fraction from radionuclide counting data. In *Nuclear Cardiology· Selected Computer Aspects.* Ed. by J. A. Sorenson (Society of Nuclear Medicine, New York), pp. 107–117.

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A comparative study of Ro 03-8799: racemic mixture and enantiomers

By Hugh F. V. Newman, F.R.C.R., *Eamonn P. Dunphy, F.R.C.R., Norman M. Bleehen, F.R.C.P., F.R.C.R., F.A.C.R., *Stanley Dische, M.D., F.R.C.R., *Michele I. Saunders, M.D., F.R.C.R., *Cheryl Des Rochers, B.Sc., S.R.N., Paul Workman, Ph.D., †Ian Lenox-Smith, M.B., B.Chir., Dip. Pharm. Med. and †Carey E. Smithen, Ph.D.

University Department and MRC Unit of Clinical Oncology and Radiotherapeutics, Cambridge CB2 2QQ,
*Marie Curie Research Wing for Oncology, Mount Vernon Hospital, Northwood, Middlesex HA6 2RN,
†Roche Products Ltd, Welwyn Garden City AL7 3AY

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ABSTRACT

The maximum single dose of the 2-nitroimidazole hypoxic cell radiosensitiser Ro 03-8799 is limited to 1 g/m^2 by the occurrence of a well characterised acute syndrome of sweating, nausea and mental changes. In an attempt to increase the tolerable dose, the clinical toxicity of the racemic mixture was compared with that of the R- and S-enantiomers of Ro 03-8799. Twelve patients received escalating alternate doses of racemic mixture and R- or S-enantiomer, the dose levels being 0.25 g/m^2, 0.5 g/m^2, 0.75 g/m^2 and 1.0 g/m^2. Careful monitoring of the acute syndrome failed to demonstrate any consistent differences between racemic mixture and either enantiomer. This would suggest that the toxicity is not mediated via any specific central nervous system receptor. It is concluded that separation of Ro 03-8799 into its enantiomers will not enable a clinically useful increase in dosage.

The maximum dose and, therefore, the clinical usefulness of nitroimidazole hypoxic cell radiosensitisers is often limited by neurotoxicity. With the (2-nitroimidazolyl)propanolamine Ro 03-8799 this consists of an acute syndrome comprising dizziness, nausea, sweating, taste abnormalities, paraesthesia and a feeling of detachment. These symptoms vary between patients, but are dose-related; the maximum single dose which may be given is 1 g/m^2 of surface area (Roberts et al, 1984; Saunders et al, 1984). The pathogenesis of this syndrome has not been elucidated.

The Ro 03-8799 substance used in clinical and most pre-clinical studies actually contains equal amounts of two distinct molecular forms known as enantiomers (Fig. 1), which together comprise the normal, so-called racemic, mixture*. The two enantiomers have been prepared separately, and found to possess equivalent radiosensitising activity and chronic aerobic cytotoxicity *in vitro* (Jones et al, 1984, personal communication). However, with some racemic compounds having central nervous system (CNS) activity the efficacy (desired activity) and toxicity (undesired activity) may reside with different enantiomers, as for several arylalkanolamines and arylalkylamines not unrelated to Ro 03-8799 (Portoghese, 1970; Simonyi, 1984). It was therefore possible that one of the enantiomers of Ro 03-8799 would be primarily responsible for the acute CNS toxicity syndrome. With equal efficacy, administration of the less toxic enantiomer might allow a useful increase in dose, and hence in the sensitisation which might be achieved. Although behavioural studies in mice and cats showed no significant difference between the enantiomers or Ro 03-8799 racemic mixture, none of these investigations detected effects which could be considered equivalent to the acute syndrome seen in man (Holmes, 1984, personal communication). Using a within-patient escalating dose regimen, we have now compared the severity of symptoms produced by the individual enantiomers of Ro 03-8799 with that of the conventional racemic mixture in man.

PATIENTS AND METHODS

Twelve patients undergoing radiotherapy were studied, six in each of our two institutions. All had normal mental function and no previous history of neurological, renal or hepatic disease. Patients who were taking benzodiazepines, glucocorticoids or enzyme-inducing agents were excluded, as were those with abnormal renal or liver function tests. Ethical Committee approval was granted for the study at both institutions and informed consent was obtained.

Methods for the preparation of Ro 03-8799 racemic mixture from racemic epichlorohydrin have been described (Smithen, 1981). Both enantiomers of Ro 03-8799 were obtained by optical resolution of the racemic mixture using either the classical method of diastereomeric salt formation with pure enantiomers of chiral acids (Wilen, 1971) or the kinetic method of stereoselective N-oxidation (Miyano et al, 1983). N-acyl derivatives of α-amino acids, such as N-phthaloylphenylalanine, are particularly useful as resolving agents for racemic bases such as Ro 03-8799 because

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*The enantiomers as seen in Fig. 1 have identical chemical formulae but differ in the spatial arrangement of the atoms, being mirror images in the plane of the paper. Enantiomers (or optical isomers) differ in their behaviour towards polarised light, and may differ profoundly in pharmacological activity.

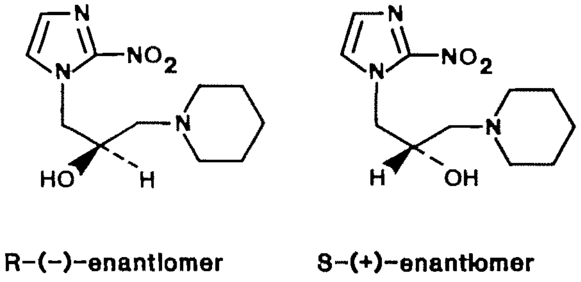

FIG. 1.

Stereostructures of enantiomers of Ro 03-8799 The enantiomers shown are mirror-images in the plane of the paper.

both enantiomers of the amino acid are readily available in high optical purity, at least one of the diastereomeric acid-addition salts is highly crystalline and easily purified by recrystallisation, and subsequent treatment of the purified salt in a conventional manner results in liberation of the corresponding enantiomer of the base and recovery of the resolving agent. Thus, N-phthaloyl-L-phenylalanine gave pure (−)-enantiomer of Ro 03-8799, $[\alpha]_D$ −6.0° ($c = 1.0$, MeOH)†. The absolute stereochemistry of the enantiomers of Ro 03-8799 was established by stereospecific syntheses from the known enantiomers of epichlorohydrin, using the methods previously described (Smithen, 1981). Thus, S-(+)-epichlorohydrin obtained from D-mannitol (Baldwin et al, 1978) gave R-(−)-enantiomer of Ro 03-8799 having > 90% enantiomeric purity†. Each enantiomer was finally converted into the corresponding hydrochloride salt.

Ro 03-8799 was administered on alternate days, to allow clearance of the previously administered drug. Dosage began at 250 mg/m^2 of racemic mixture, followed by the same dose of either R- or S-enantiomer on a double-blind basis. The drugs were infused in 50 ml of normal saline over 10 min, and the patients carefully observed for any subjective or objective toxicity. The dose was escalated through 500 mg/m^2 and 750 mg/m^2 to 1 g/m^2, each individual patient receiving the same enantiomer throughout. All doses refer to the hydrochloride salt.

Side-effects were graded as:

(0) no side-effects;
(1) mild: causing little or no distress and not requiring any modification of the infusion or special treatment;
(2) moderate: causing some distress, and possibly needing slowing of the infusion but not needing special care; and
(3) severe: causing marked distress, needing special care or discontinuing the infusion

Full blood count, urea, electrolytes, creatinine and liver function tests were monitored during and 1 month after administration of the radiosensitiser, and patients were also followed up for evidence of any other toxicity.

Fractional urine collections were made from all 12 patients for determination of urinary recovery patterns at matching doses of racemic mixture and enantiomers and four patients had paired plasma pharmacokinetics performed. Analysis was by paired-ion reversed-phase high-performance liquid chromatography, using published methods (Malcolm et al, 1983).

RESULTS

The expected acute syndrome was seen to some extent in all but one of the 12 patients. The exception had no toxicity at any dose level of either mixture or S-enantiomer. As can be seen in Table I, the acute toxicity increased with escalating doses, but there was no consistent difference in toxicity between racemic mixture and either enantiomer. One patient who had an inadvertently rapid infusion of racemic mixture at 500 mg/m^2 experienced side-effects as severe as with 1 g/m^2 infused over 10 min. This is consistent with similar effects seen in larger series (Roberts et al, 1984) and suggests that rapid peak plasma levels may be an important factor in the acute toxicity of Ro 03-8799. One patient did not receive the final dose of R-enantiomer owing to very severe side-effects at 1 g/m^2 of mixture, and one patient completed the escalation above 750 mg/m^2 with racemic mixture only, owing to the stock of S-enantiomer being exhausted.

There was no late toxicity observed in terms of central or peripheral neuropathy, nephropathy or hepatopathy, with follow-up times of 1–5 months following drug administration. Three patients have subsequently died from metastasis or other causes unrelated to Ro 03-8799.

Two sets of paired fractional urine collections analysed have shown similar urinary recoveries for mixture, R- and S-enantiomer. More detailed pharmacology will be described elsewhere.

DISCUSSION

A differential distribution of toxicity between the two enantiomers would have resulted in one being more toxic and the other less toxic than the racemic mixture. Although the number of patients who could be studied is small owing to very limited availability of the enantiomers, we would have expected to detect any marked differential likely to allow a substantial dose increase.

There is ample precedent that the enantiomers of other arylalkanolamines having CNS activity, such as those which act at the adrenergic receptors, often show significant differential effects (Simonyi, 1984). It is widely assumed that the close proximity of the asymmetric (chiral) centre of such molecules to the site

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†Full experimental details of the resolution of Ro 03-8799 racemic mixture, stereospecific syntheses of the enantiomers and methods of assay of enantiomeric purity will be described elsewhere by Smithen et al.

TABLE I

TOXICITY RATINGS AT ESCALATING DOSES OF RO 03-8799 MIXTURE AND ENANTIOMERS

Case	Enantiomer given	Dose, mg/m^2							
		250		500		750		1000	
		Racemic	Enantiomer	Racemic	Enantiomer	Racemic	Enantiomer	Racemic	Enantiomer
1	R-enantiomer	0	0	1	1	1	1	1	2
2		1	1	2	1	1	1	2	2
3		0	0	1	0	2	0	3	NG
4		0	0	0	0	0	0	2	2
5		0	0	1	0	2	1	3	2
6		1	1	1	1	2	2	3	3
7	S-enantiomer	1	1	2	1	1	1	1	1
8		0	0	0	0	0	0	0	0
9		0	0	0	0	2	3	2	2
10		0	0	0	0	1	1	1	1
11		0	0	1	1	3	2[a]	2[a]	2[a]
12		0	0	3[b]	2	2	2	3	3

0, none; 1, mild, 2, moderate, 3, severe; NG, not given; [a]racemic mixture only at $\geqslant$ 750 mg/m^2, [b]rapid infusion.

of receptor binding is responsible for these differences. The failure to detect any significant differences in the pharmacological effects of the separated and mixed enantiomers of the (2-nitroimidazolyl)propanolamine Ro 03-8799, either in the present clinical study or in earlier animal studies (Holmes, 1984, personal communication), suggests that the acute syndrome observed in man is unlikely to involve any specific CNS–receptor interaction.

It is concluded that the separation of Ro 03-8799 into its enantiomers is unlikely to enable a large increase in individual doses of this agent. It is possible that small differences in acute toxicity may not have been detected, but the clinical advantage which might accrue from minor dose escalation is uncertain, and further investigation of this approach is not justified. Other approaches to improve the clinical utility of Ro 03-8799 should be investigated. It may be more rewarding to pursue the approach of combining Ro 03-8799 with a less lipophilic nitroimidazole possessing different toxicities, in order to achieve a greater combined radiosensitising effect

REFERENCES

BALDWIN, J. J., RAAB, A. W., MENSLER, K., ARISON, B. H. & MCCLURE, D. E., 1978. Synthesis of (R)- and (S)-epichlorohydrin. *Journal of Organic Chemistry, 43,* 4876–4878.

MALCOLM, S. L., LEE, A. & GROVES, J. K., 1983 HPLC analysis of Ro 03-8799 in biological samples. *Journal of Chromatography, 273,* 327–333.

MIYANO, S., LU, L D. L., VITI, S. M. & SHARPLESS, K. B., 1983. Kinetic resolution of racemic beta-hydroxy amines by enantioselective N-oxide formation. *Journal of Organic Chemistry, 48,* 3608–3611

PORTOGHESE, P. S., 1970. Relationships between stereostructure and pharmacological activities. In *Annual Review of Pharmacology 10.* Ed. by H W. Elliot, W C Cutting & R. H Dreisbach (Annual Reviews Inc., Palo Alto, California), pp. 51–76.

ROBERTS, J. T., BLEEHEN, N. M, WORKMAN, P & WALTON, M I, 1984. A phase I study of the hypoxic cell radiosensitizer Ro 03-8799 *International Journal of Radiation Oncology, Biology, Physics, 10,* 1755–1758.

SAUNDERS, M I, ANDERSON, P. J., BENNETT, M. H., DISCHE, S., MINCHINTON, A., STRATFORD, M R. L. & TOTHILL, M, 1984. The clinical testing of Ro 03-8799—pharmacokinetics, toxicology, tissue and tumor concentrations. *International Journal of Radiation Oncology, Biology, Physics, 10,* 1759–1763.

SIMONYI, M., 1984. On chiral drug action. *Medical Research Reviews, 4,* 359–413

SMITHEN, C. E., 1981 (F. Hoffmann-La Roche and Co AG). New nitroimidazoles European patent 0000928.

WILEN, S. H., 1971. Resolving agents and resolutions in organic chemistry. In *Topics in Stereochemistry 6.* Ed. by N L Allinger & E L. Eliel (Wiley Interscience, New York), pp. 107–176.

Book review

Optimization of Cancer Radiotherapy. Proceedings of the Second International Conference on Dose, Time and Fractionation in Radiation Oncology, September 12–14, 1984, Madison, Wisconsin. Ed. by Bhudatt R. Paliwal, Donald E. Herbert and Colin Orton, pp. 538, 1985 (American Institute of Physics for the American Association of Physicists in Medicine), $45.00/$30.00 AAPM members.
ISBN 0–88318–483–4

This publication presents the proceedings of a symposium held at the University of Wisconsin in September 1984. The objective of the three-day symposium was to provide a forum for radiation biologists, medical physicists, oncologists, dosimetrists, computer scientists and manufacturers of radiation therapy equipment to discuss radiobiological, physical and clinical aspects of time, dose and volume effects on precise and optimised management of cancer therapy.

Although this is a book of the proceedings of a conference and, inevitably, suffers from the fact that it is a set of individual papers from authors with their own styles, it does form a useful, comprehensive review of the subject. The subject, however, is definitely that of the conference title, being much more concerned with fractionation and radiobiological considerations than with dose distribution concepts, although there is a mixed section of papers on this subject in the last section of the book.

The proceedings have been divided into four main sections: (1) treatment strategies: clinical; (2) treatment strategies. radiobiological considerations; (3) time, dose and volume models and recent developments; (4) treatment planning optimisation.

Treatment strategies (clinical) covers a range of new clinical approaches including: hyperfractionation split-course, low- and high-dose-rate brachytherapy, combination therapy and neutrons, with excellent papers from major centres of radiotherapy/oncology in the United States.

Treatment strategies (radiobiological) is a set of papers mainly dealing with the practical aspects of radiobiology but also including some clinical work. The papers are all from North America except for one from Rotterdam on high-dose-rate remote afterloading and another from Bombay on time dose fractionation factors for tumours.

Time, dose and volume models is the predominant section of the book—approximately 200 pages—with detailed discussion of all the various radiobiological models. There is one paper in particular, taking 70 pages, by D. E. Herbert, "a general linear model of clinical radiation effects", which weighs the book down by its statistical analysis of the subject and is so like a thesis that it is difficult to believe that it formed a conference lecture. However, the subjects relevant to radiotherapy are well covered in breadth as well as in depth, so that there is something for everyone. All of the authors, except for Turesson, are from North America.

Treatment planning optimisation includes a few papers on the subject of optimisation of interest to physicists—techniques to improve dose distributions—that are practically based. The others are "bioeffect" semitheoretical papers, plus an "oddball" paper on the use of californium-252 needles.

This is a useful book, mainly as a source of reference to the radiobiological models that are in vogue at the present time. Given the title of the book, I would like to have seen more papers on the very important practical subject of treatment planning optimisation, but perhaps this should form a book of its own.

E. G. A. Aird

1986, *The British Journal of Radiology*, 59, 1001–1005 October 1986

A comparative study of dose distribution of a high-energy electron beam and chromosome aberration frequencies

By Sho Matsubara, M.D., Yuji Kuwabara, M.D., Junichi Horiuch, M.D., Soji Suzuki, M.D., Masao Hoshina, B.Sc. and Tsuguhisa Kato, B.Sc.

Department of Radiology, Tokyo Medical and Dental University, School of Medicine, 1-5-45, Yushima, Bunkyo-ku, Tokyo 113, Japan

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Abstract

Electron beam therapy is usually employed for the treatment of tumours located at or near the surface of the body, because the electron beam gives a high dose near the surface, but falls off rapidly with increasing depth beyond the level of the 80% depth dose. Isodose curves for radiotherapy have been obtained using physical methods, but have rarely been investigated on the basis of living human cells. In the present study, lymphocyte chromosome analysis was employed as a biological dosemeter for comparison with the isodose curve measured physically. The peripheral blood was exposed to a 14 MeV electron beam in a plastic tube set in a specially made test-tube stand immersed in a water tank. The chromosome aberration frequencies induced by irradiation of about 95% of peak dose at a depth of 31 mm were found to be higher in value than those induced at a depth of 17 mm where the peak dose had been determined physically. Three gray of irradiation given to whole blood in the presence of contrast medium gave rise to a slight enhancement of radiation-induced chromosome aberration frequencies in the lymphocytes exposed at a depth of 17 mm, but a slight decrease at 31 mm.

It has been said that the advantage of high-energy electron beam therapy is that the electrons have a limited range in tissue, so that a suitable energy level can be selected to carry them to the desired site of irradiation without damaging the deeper tissues. Electron therapy is, therefore, usually employed in the treatment of tumours located near the body surface. In undertaking electron therapy, adequate knowledge is required concerning the build-up of the absorbed dose, which decreases in degree as the energy used is increased (Ovadia & Uhlmann, 1960; Loevinger et al, 1961; Zatz et al, 1961; International Commission on Radiation Units and Measurements (ICRU), 1972, 1979). It has been generally believed that there is no gross difference in the relative biological effectiveness (RBE) along the dose distribution in high-energy electron beam therapy (Leskowitz et al, 1960; Schmid et al, 1974). In the present investigation we have compared the absorbed dose obtained by a physical method with that obtained using chromosome aberration frequencies as a biological dosemeter (Sasaki, 1971; Dolphin et al, 1973; Matsubara et al, 1974; Schmid et al, 1974; Silberstein et al, 1974). Furthermore, the absorbed dose of the electron beam depends upon the electron density and atomic number of the irradiated materials, resulting in an increased absorbed dose in osseous tissue (Laughlin et al, 1965; Almond et al, 1967; Khan et al, 1978; Hogstrom et al, 1981; Prasad et al, 1984). Therefore the effect of contrast medium on the chromosome aberration induction in lymphocytes (Adams et al, 1977; Matsudaira et al, 1980; Matsubara et al, 1982, 1984) with electron beam exposure was also investigated.

Materials and Methods

Exposure to high-energy electron beam

The venous blood was taken from young healthy persons who did not have any previous history of exposure to ionising radiation. The blood was irradiated, in plastic tubes (inner diameter 14 mm and 10 mm, No. 2037 and No. 2058, respectively, Falcon) immersed in water in a small tank made of acrylic resin, by a betatron unit (20-AE, Shimadzu). In the first study of the dose–effect relationship, the blood was injected into the 14 mm plastic tube, and the irradiation was given laterally at a position 22 mm from the surface of the water tank to the midpoint of the tube through a 12 cm × 12 cm portal at an energy of 14 MeV and a dose-rate of 3.38 Gy/min. On the other hand, in the investigation of dose distribution, the thinner plastic tubes with 10 mm inner diameter were set up in a test-tube rack of acrylic resin, which was specially made for irradiation at 17 mm, 31 mm, 37 mm, 46 mm and 55 mm from the surface of the water tank to the midpoint of each tube exposed to the 14 MeV electron beam through a 12 cm × 12 cm lateral portal in the water (Fig. 1). The physical dose distribution in the water, measured by an Ionex 0.6 ml chamber (Type 2500/3, Nuclear Enterprises), showed that the beam was reasonably flat (a maximum variation of 7%). The irradiation was performed according to the method described below.

(1) Lymphocytes were irradiated with from 0.25 Gy to 3.96 Gy in the larger test-tubes with an inner diameter of 14 mm at a depth of 22 mm, and the dose–effect relation was compared with that of ^{60}Co γ rays. The absorbed doses at 22 mm depth were estimated by a correction (99%) from the peak value at 17 mm depth derived from the physical depth–dose curve.

(2) Three gray of irradiation was given to the peripheral lymphocytes in test-tubes with an inner diameter of 10 mm at various depths, as described

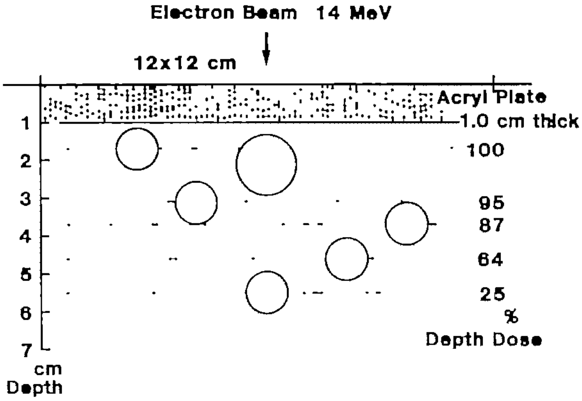

FIG. 1.

The peripheral blood contained in plastic tubes was irradiated by a 14 MeV electron beam in the specially designed test-tube rack immersed in a water tank. The large circle indicates a test-tube with a 14 mm inner diameter, the small circles those with a 10 mm inner diameter

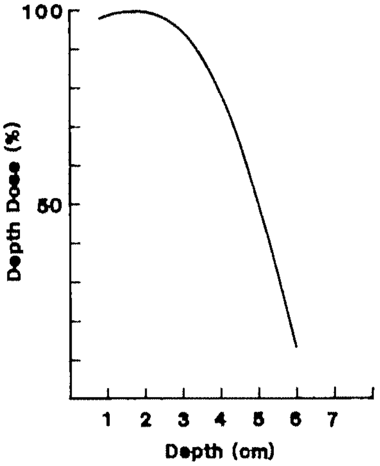

FIG. 2.

The dose distribution of a 14 MeV electron beam measured by an Ionex 0.6 ml chamber within water. The peak dose is at 17 mm depth and 80% at 40 mm depth.

above. The absorbed doses given in this and subsequent irradiations were measured at a peak dose site of 17 mm depth.

(3) In order to investigate the chromosome aberration induction efficiencies in the lymphocytes irradiated within the shoulder of the electron beam, the following irradiations were done at depths of 17 mm and 31 mm: Experiment (a) 0.5 Gy, 1.0 Gy, 2.0 Gy and 4.0 Gy, Experiment (b) 3.0 Gy and 9.0 Gy.

(4) Additionally, 3 Gy of electron beam exposure was given to peripheral lymphocytes in the presence of contrast medium (iothalamate (Conray): meglumine-5-acetamido-*N*-methyl-2,4,6-triiodo-isophthalamate) to ascertain its effect. The concentration of iodine employed was 4%.

Lymphocyte culture, slide preparation and chromosome analysis

The whole blood was cultivated in RPMI-1640 culture medium with 20% fetal bovine serum after the addition of 0.2 ml of PHA (phytohaemagglutinin, M-type). In order to ensure that only first division cells were analysed, the fluorescence-plus-Giemsa (FPG) staining technique would have been much better. However, Colcemid (demecolcine) was added at the final concentration of 0.5 μg/ml 24 h after the initiation of incubation at 37°C to facilitate comparison with Sasaki's previous data (1971). The lymphocytes were harvested at 50 h cultivation. Following treatment with 0.075 M KCl solution and fixation, the flame-dried preparation slides were stained with Giemsa.

Dicentric or polycentric chromosomes and ring chromosomes were employed in the present study because they could be easily scored without mistakes and they are commonly appreciated as a biological dosemeter. Slides were coded before being scored. The number of cells analysed ranged from 100 to 300, and larger numbers of cells were observed in the lower radiation dose ranges. For the analysis of the dose–response relationship, the data were fitted by least-squares regression analysis to a linear-quadratic model. The statistical significance of chromosome aberration frequencies was estimated by the difference between the two population proportions.

RESULTS

The depth–dose curve of the 14 MeV electron beam in water measured by the ionisation chamber (Fig. 2) showed a maximum absorbed dose at a depth of 17 mm and the 80% point at 40 mm depth forming a smooth shoulder configuration. The whole blood was irradiated with from 0.25 Gy to 3.96 Gy in a test-tube with a 14 mm inner diameter, which was set at a depth of 22 mm from the surface of the water tank. The variation of chromosome aberration frequencies with radiation dose was quite compatible with that obtained with ^{60}Co γ-ray irradiation (Fig. 3) and was found to be expressed by a linear quadratic model:

$$Y = 1.14\times10^{-2}\times D + 6.83\times10^{-2}\times D^2 \qquad (1)$$

where Y and D indicated yields of dicentrics plus rings and dose in Gy, respectively.

The chromosome aberration frequencies induced by 3 Gy irradiation in the test-tubes with 10 mm inner diameter were obtained for various depths and illustrated in the form of relative chromosome aberration frequencies, in comparison with the estimated values calculated by substituting the dose at each depth in Equation (1) (Fig. 4). The curve of estimated chromosome aberration frequencies, thus obtained, showed a gentle smooth shoulder with a peak

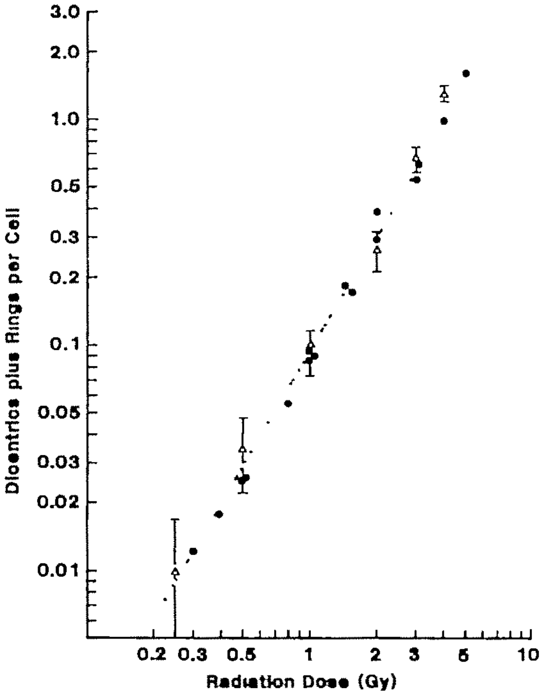

Fig. 3

The chromosome aberration frequency versus radiation dose obtained by 14 MeV electron irradiation within a test-tube of 14 mm inner diameter (open triangles) is compatible with that obtained by ^{60}Co γ-ray irradiation (closed circles along the dotted line) previously reported by Sasaki (1971).

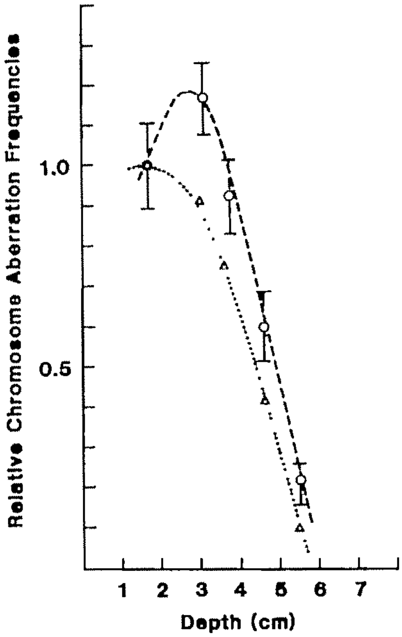

Fig. 4

Relative chromosomal aberration frequencies obtained by 3 Gy irradiation of blood in the test-tubes with an inner diameter of 10 mm at 17 mm, 31 mm, 37 mm, 46 mm and 55 mm depth are shown by open circles along the broken line. The estimated chromosome aberration frequencies converted from the physical doses are shown by open triangles with dotted line. Vertical lines show standard errors.

at 17 mm and a rapid fall-off in frequencies with depths beyond about 30 mm. On the other hand, the depth–effect curve based upon the observed chromosome aberration frequencies was very different. The aberration frequencies induced by about 95% of peak dose at the 31 mm depth were found to be about 17% higher in value than those induced by the peak dose determined physically at 17 mm depth. The ratios of observed aberration frequencies to the estimated ones are listed in Table I.

TABLE I

The relation between estimated and observed chromosome aberration frequencies at various depths

Depths (mm)	Relative chromosome aberration frequencies		Ratios
	Estimated values	Observed values	
17	1.0	1.0	1.0
31	0 91	1.17	1.29
37	0.75	0.92	1.23
46	0.42	0 6	1 43
55	0 1	0.22	2.2

We therefore repeated the whole-blood irradiation in the thinner test-tubes (10 mm inner diameter), which were set in the test-tube stand at 17 mm and 31 mm from the surface of the water tank. In all of these

TABLE II

14 MeV electron beam irradiation and chromosome aberrations

Experiment	Radiation dose (Gy)	No. of cells scored	Dicentric plus rings		Significance (p)
Irradiation position at 17 mm depth					
(a)	0 5	300	8	0.027 ± 0.009	>0.05
	1.0	300	25	0.083 ± 0.017	>0.05
	2.0	300	83	0.28 ± 0.03	>0.05
	4.0	200	200	1.0 ± 0.07	>0.05
(b)	3.0	250	106	0 42 ± 0.04	<0 05
	9.0	100	300	3.00 ± 0 17	>0.05
Irradiation position at 31 mm depth					
(a)	0 5	300	13	0.043 ± 0 012	
	1.0	300	35	0.11 ± 0 02	
	2.0	300	102	0.34 ± 0.03	
	4.0	200	229	1.15 ± 0.08	
(b)	3.0	250	129	0.52 ± 0.05	
	9.0	100	330	3 30 ± 0 18	

TABLE III

THE EFFECT OF CONTRAST MEDIUM ON THE DISTRIBUTION OF RADIATION-INDUCED CHROMOSOME ABERRATION FREQUENCIES AGAINST DEPTH

Depth (mm)	No. of cells scored	Dicentric plus rings		Significance (p)
Irradiation without contrast medium				
17	200	84	0.42 ± 0.05	<0.05
31	200	106	0.53 ± 0.04	<0.05
37	200	79	0.40 ± 0.04	>0.05
46	200	54	0.27 ± 0.04	>0.05
55	200	16	0.08 ± 0.02	>0.05
Irradiation with contrast medium				
17	200	122	0.61 ± 0.06	
31	200	86	0.43 ± 0.05	
37	200	73	0.37 ± 0.04	
46	200	41	0.21 ± 0.03	
55	200	11	0.06 ± 0.02	

comparative irradiation experiments with 0.5–9.0 Gy at the 17 mm-deep peak dose, the chromosome aberration frequencies were found to be from 10% to 60% more at a depth of 31 mm than at 17 mm, though the differences were not statistically significant except for one pair of irradiations (Table II, experimental doses (a) and (b)). As for the dose–effect relationships, seen in Table II, Experiment (a), two equations were obtained:

$$Y = 2.96 \times 10^{-2} \times D + 5.54 \times 10^{-2} \times D^2 \qquad (2)$$

$$Y = 4.47 \times 10^{-2} \times D + 6.07 \times 10^{-2} \times D^2 \qquad (3)$$

at 17 mm and 31 mm from the surface of the water tank, respectively. The yield of dicentrics and rings obtained in the irradiation at a depth of 31 mm were revealed to be slightly higher.

Furthermore, in the experiment with 3 Gy irradiation of whole blood in the presence of contrast medium (4% iodine) an enhancement of radiation-induced chromosome aberration frequencies was noted in the lymphocytes exposed at 17 mm, while a decrease in aberration frequencies was demonstrated at deeper sites, especially at 31 mm. The enhancement ratio at 17 mm was about 1.45 (Table III).

DISCUSSION

In the present study, instead of using dosimetric chambers, the peripheral blood lymphocytes placed in plastic tubes were set up at various depths in a test-tube rack immersed in a water tank and exposed to an electron beam. Chromosome analysis has frequently been used in the field of radiation hazard and protection in order to estimate an equivalent whole-body dose. However, the technique has rarely been used as a biological dosemeter to make an isodose curve for radiotherapy, although Lloyd et al (1978) employed chromosome aberration analysis as a biological dosemeter and studied the biological effectiveness of negative pi-mesons in an experimental exposure. The biological effectiveness of high-energy electron beam irradiation is generally believed to be equal to that of ^{60}Co γ-ray irradiation. The effectiveness of 20 MeV electrons has been calculated to be 0.82 relative to 180 kVp X rays (Leskowitz et al, 1960). On the isodose curve in homogeneous tissue, the peak dose region occurs deeper as electron energy increases and is usually located between 10 mm and 30 mm deep in the cases of irradiation with electron beams of 10 MeV to 50 MeV (ICRU, 1972, 1979). The depth of the 80% isodose area is about $E/30$ mm in the case of irradiation with an electron beam of energy E MeV.

In order to investigate the actual radiological effect on living cells, we employed chromosome aberration analysis as a biological dosemeter and compared it with an ionisation chamber. The depth doses measured by the chamber were converted to the estimated chromosome aberration frequencies by substituting the dose at each depth in Equation (1) and the observed chromosome aberration frequencies were higher than the estimated values at a depth of 31 mm and deeper sites (Fig. 4 and Table I). The statistical evaluation of aberration frequencies obtained in the comparative experiment at 17 mm and 31 mm depth areas revealed some differences with and without statistical significance, although all cases showed higher frequencies of the order of 10% to 60% at the 31 mm depth area (Table II, Experiments (a) and (b)). It may be hard to draw the conclusion from this small investigation that the difference between estimated chromosome aberration frequencies based upon physically measured absorbed doses and observed ones at various depths was due to an increased biological effect or RBE (Leskowitz et al, 1960; Schmid et al, 1974), although a slight difference was disclosed in chromosome aberration yields and their slopes between the two dose–effect curves obtained at 17 mm and 31 mm depths from Equations (2) and (3). The effect of a dose-dependent selection mechanism, for example, division delay and/or interphase death (Sharpe, 1969; Lloyd et al, 1977), may give rise to some distortion in the dose–effect relationship of chromosome aberration frequencies. Furthermore, the inadequacy of physical dosimetry using an Ionex 0.6 ml chamber for this electron beam cannot be excluded.

The dose distribution of the high-energy electron beam is easily influenced by the presence of material inhomogeneous in electron density and atomic number in the irradiated tissue. In electron beam therapy, bony tissue and air in organs are reported to give rise to the distortion of dose distribution curves (Laughlin et al, 1965; Almond et al, 1967; Khan et al, 1978; Hogstrom et al, 1981; Prasad et al, 1984). In the present study with contrast medium, we could find the enhancement phenomenon in the irradiation with 3 Gy at 17 mm, but not at deeper sites, especially not at 31 mm (Table III). The dose–effect curve seemed to be shifted towards the left to a slight degree. The interaction between electron particles and iodine atoms from the contrast medium at various levels of energy is to be investigated further in order to obtain more precise knowledge concerning this problem.

In electron beam therapy, the level of energy of 14 MeV is recognised as making a smooth shoulder in the dose distribution curve as far as about 40 mm in depth without much build-up. On the other hand, our chromosome aberration analysis showed a difference in yields in the lymphocytes irradiated at depths of 17 mm and 31 mm. These results may suggest a higher radiation effect at slightly deeper sites in the tissue than those so far considered. The dose distribution curve is usually obtained by a physical method and applied directly to the technique of radiotherapy. However, the biological method directly using human living cells can check the actual effects of radiation. Among biological dosemeters (ICRU, 1979), chromosome analysis is said to be the best for its simplicity and accuracy, and it will be of great value in making a dose distribution curve in radiotherapy, especially using other particle radiation.

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REFERENCES

Adams, F. H., Norman, A., Mello, R. S. & Bass, D., 1977. Effect of radiation and contrast media on chromosomes: Preliminary report. *Radiology, 124,* 823–826.

Almond, P. R., Wright, A. E. & Boone, M. L. M., 1967. High-energy electron dose perturbations in regions of tissue heterogeneity. *Radiology, 88,* 1146–1153.

Dolphin, G. W., Lloyd, D. C. & Purrott, R. J., 1973. Chromosome aberration analysis as a dosimetric technique in radiological protection. *Health Physics, 25,* 7–15.

Hogstrom, K. R., Mills, M. D. & Almond, P. R., 1981. Electron beam dose calculations. *Physics in Medicine and Biology, 26,* 445–459.

ICRU, 1972. Radiation dosimetry: electrons with initial energies between 1 and 50 MeV. *ICRU Report 21.* (ICRU, Washington, DC).

—1979. Quantitative concepts and dosimetry in radiobiology. *ICRU Report 30.* (ICRU, Washington, DC).

Khan, F. M., Sewchand, W. & Levitt, S. H., 1978. Effect of air space on depth dose in electron beam therapy. *Radiology, 126,* 249–251.

Laughlin, J. S., Lundy, A., Phillips, R., Chu, F. & Sattar, A., 1965. Electron-beam treatment planning in inhomogeneous tissue. *Radiology, 85,* 524–531.

Leskowitz, I., Van Dyke, J. G., Laughlin, J. S. & Nickson, J. J., 1960. The relative biological efficiency of 20-MeV electrons and 180-kVp x-rays in *Escherichia coli* inactivation. *Radiation Research, 13,* 445–451.

Lloyd, D. C., Dolphin, G. W., Purrott, R. J. & Tipper, P. A., 1977. The effect of x-ray induced mitotic delay on chromosome aberration yields in human lymphocytes. *Mutation Research, 42,* 401–412.

Lloyd, D. C., Reading, D. H., Purrott, R. J., Hynes, M. A., Spinks, W. S. & Stephenson, B. D., 1978. Expansion of a negative pi-meson peak to cover a range of depths useful for radiotherapy. *British Journal of Radiology, 51,* 41–45.

Loevinger, R., Karzmark, C. J. & Weissbluth, M., 1961. Radiation therapy with high-energy electrons. Part I. Physical considerations, 10 to 60 MeV. *Radiology, 77,* 906–926.

Matsubara, S., Sasaki, M. S. & Adachi, T., 1974. Dose–response relationship of lymphocyte chromosome aberrations in locally irradiated persons. *Journal of Radiation Research, 15,* 189–196.

Matsubara, S., Suzuki, S., Suzuki, H., Kuwabara, Y. & Okano, T., 1982. Effects of contrast medium on radiation induced chromosome aberrations. *Radiology, 144,* 295–301.

Matsubara, S., Suzuki, S. & Kuwabara, Y., 1984. The effects of diagnostic x-ray and contrast media on lymphocyte chromosomes. *Fortschritte auf dem Gebiete der Röntgenstrahlen und der Nuklearmedizin, 140,* 215–219.

Matsudaira, H., Ueno, A. M. & Furuno, I., 1980. Iodine contrast medium sensitizes cultured mammalian cells to x-rays but not to γ-rays. *Radiation Research, 84,* 144–148.

Ovadia, J. & Uhlmann, E. M., 1960. Isodose distribution and treatment planning with electrons of 20–35 MeV for deep-seated tumors. *American Journal of Roentgenology, 84,* 754–760.

Prasad, S. C., Ames, T. E., Howard, T. B., Bassano, D. A., Chung, C. T., King, G. A. & Sagerman, R. H., 1984. Dose enhancement in bone in electron beam therapy. *Radiology, 151,* 513–516.

Sasaki, M. S., 1971. Radiation-induced chromosome aberrations in lymphocytes: possible biological dosimeter in man. In *Biological Aspects of Radiation Protection.* Ed. by T. Sugahara & O. Hug (Igaku Shoin, Toyko), pp. 81–91.

Schmid, E., Rimpl, G. & Bauchinger, M., 1974. Dose–response relation of chromosome aberrations in human lymphocytes after in vitro irradiation with 3 MeV electrons. *Radiation Research, 57,* 228–238.

Sharpe, H. B. A., 1969. Pitfalls in the use of chromosome aberration analysis for biological radiation dosimetry. *British Journal of Radiology, 42,* 943–944.

Silberstein, E. B., Ewing, C. J., Bahr, G. K. & Kereiakes, J. G., 1974. The human lymphocyte as a radiobiological dosimeter after total body irradiation. *Radiation Research, 59,* 658–664.

Zatz, L. M., Essen, C. F. & Kaplan, H. S., 1961. Radiation therapy with high-energy electrons. Part II. Clinical experience, 10 to 40 MeV. *Radiology, 77,* 928–939.

Book reviews

Thermological Methods. Ed. by J.-M Engel, U. Flesch and G. Stuttgen, pp. 326, 1985 (VCH Verlagsgesellschaft, Weinheim, FRG), DM 136.
ISBN 3-527-15168-0 (FRG)
0-89573-410-9 (USA)

This book, by a number of distinguished European contributors, describes the scientific principles and practical methods of thermology (defined as the study of the nature and effects of thermal energy).

The opening chapters deal with the basic physiological and physical aspects of skin temperature and methods of measurement. Liquid crystal thermography is well covered, but it has limited value even when, through experience, an "intuitive skill" has improved interpretation On quantitative infra-red thermography it is claimed that the physical principles of instrument design augmented by microprocessing would open new perspectives if such powerful microprocessor technology becomes affordable in terms of cost-effectiveness. The THERMOTON system and the modified BOFORS unit are clearly of value to the rheumatologist. Also, the exquisitely fine detail of the high-performance SPRITE infra-red detector is very impressive but, again, the possibility of future clinical development is overshadowed by the cost of hardware.

The physical laws of microwave thermography and the microwave properties of body tissue are well illustrated, but the varied dielectric constants of heterogeneous body tissues complicate the achievement of accurate radiometry. Similar problems occupy the oncologist using hyperthermia in tumour treatment, and it is disappointing to discover that ultrasound thermometry of the deep tissues, correlating temperature changes with changes in sound absorption or velocity, is unlikely to provide the much-needed information sought by users of hyperthermia.

In the section on thermological measurement in clinical practice the classical Strasburg qualitative and quantitative evaluation of breast thermograms is followed by the protocol for a new interpretative scoring system. A single page describes intraoperative myocardial thermography, which could prove to be a most invaluable clinical application as the demonstration of differential cooling of the myocardium during cardioplegia is of immense importance to cardiologists.

It is not easy to summarise this well produced, accurately translated, multiauthor volume. Inevitably there is some overlap and duplication of physical data and methods of patient preparation. It fulfils its intention "to survey the scientific fundamentals and methods of thermology". Apart from medical physicists and rheumatologists, the contents will have limited appeal. Diagnostic radiologists will not be distracted from their preoccupation with CT, MRI, etc. Some of us will await the clinical yield from the newer, ingeniously designed, but costly, thermology, but the disenchantment of our early experience with thermography leaves reservations which will not readily be overcome.

D. K. L. DAVIES

Consensus Development Conference on Limb-sparing Treatment of Adult Soft Tissue Sarcomas and Osteosarcomas Cancer Treatment Symposia, Vol. 3. Ed. by R. E. Wittes, pp. 168, 1985 (US Department of Health), $8.15 (foreign).
Stock No. 017-042-00185-4

This report is one of a regular series of "Consensus Development" conferences which are held under the auspices of the National Institutes of Health in the USA. Various groups are invited to present data on topics pertinent to the subject and their contributions published along with an independent analysis of the data to arrive at the "consensus", *i.e.* what the average doctor should do.

In this case the topics were to do with limb-sparing treatment in sarcoma. The subjects covered include staging, indications for limb-sparing surgery, optional surgical treatment, need for radiation and chemotherapy, long-term functional results of conservative surgery and further directions for research.

In the main, conclusions seem reasonably sensible and some of the papers are very good The basis of staging systems for soft-tissue and bone sarcomas is discussed by Suit et al, who recommend the use of three histological grades for soft-bone sarcoma. The roles of radiotherapy and chemotherapy are described in several papers In osteosarcoma the contributions are rather pedestrian and very parochial. Many potential contributors with great knowledge and experience were not present and the data presented, although of interest, do not present a well rounded picture.

Nevertheless, the volume is worthwhile and a useful addition to a departmental library

R L SOUHAMI

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An on-line electronic portal imaging system for external beam radiotherapy

By K. S. Lam, Ph.D., *M. Partowmah, Ph.D. and W. C. Lam, Ph.D.
Department of Radiation Oncology, The Johns Hopkins Medical Institute, Baltimore, Maryland 21205, USA

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ABSTRACT

A digital imaging system has been constructed to obtain the treatment portal image of a patient during external beam radiotherapy. A DEC LSI-11/23 microcomputer controls a stepper motor, which moves a linear array of 256 silicon diodes to scan the radiation transmitted through the patient. The computer also processes the collected data to generate an image for displaying on a video monitor. The quality of the digital image is comparable to that of the conventional verification radiographs. Major advantages of the system include the speed and simplicity in data storage and retrieval and in its capability of direct comparison with simulation radiographs.

In external beam radiotherapy, the aim is to deliver a prescribed dose of radiation to the tumour while trying to minimise the radiation given to normal tissues, especially to vital organs. Prior to treatment, the patient is set up under an X-ray simulator to determine the target area to be irradiated and a simulation radiograph is taken. Shielding blocks to protect vital organs are made according to the region of interest delineated on the radiograph by the physician. To check the set-up, a portal radiograph is taken with a short burst of radiation and compared with the simulation radiograph. This procedure is carried out prior to the first treatment and thereafter only once a week (see, for example, Byhardt et al, 1978). For complex fields, verification radiographs which record the exit dose during an entire treatment have also been used. However, because X-ray films are costly and their processing is time-consuming, radiography has not been used as a routine procedure during every treatment. Nevertheless, even occasional localisation and verification radiographs have helped to identify and correct field placement errors (Marks et al, 1974, 1976).

Some studies have been carried out to monitor patient movement during radiotherapy (Kelsey et al, 1972; Norwood & Stubbs, 1984). However, because the monitoring procedure itself could make the patient conscious of the movement, unbiased results were probably difficult to obtain (Kelsey et al, 1972).

This paper describes a digital imaging system which records the treatment portal of the patient for the entire duration of the irradiation of a fixed field. The system consists of a DEC LSI-11/23 computer which controls the movement of a linear array of diode detectors to scan the radiation passing through the patient. The signals from the detectors are processed to produce an image which appears on a video monitor during the irradiation. The collected digital data are stored on a floppy disk for analysis at a later time. The image quality of the system is illustrated with results from phantom measurements and examples from a patient study.

THE ELECTRONIC PORTAL IMAGING SYSTEM

Hardware configuration

A block diagram of the electronic portal imaging system is shown in Fig. 1. It is under the programmed control of a DEC LSI-11/23 microcomputer which has a memory of 128K words and two floppy disk drives for program and data storage. The computer coordinates the data collection and the scanning of the radiation transmitted through the patient. The design is based on the technique of using a diode array to scan a radiation field (Taborsky et al, 1982); this study showed that silicon diodes have a sufficiently good signal-to-noise ratio to delineate bony landmarks. The present system consists of a linear array of 256 silicon diodes which are mounted on a rigid frame that is carried by two guide-rails. The frame is positioned by a timing belt and grooved pulley system driven by a stepper motor. The centre-to-centre separation between adjacent diodes is 2 mm. To obtain the maximum output signal for a given amount of radiation, a layer of lead is placed on

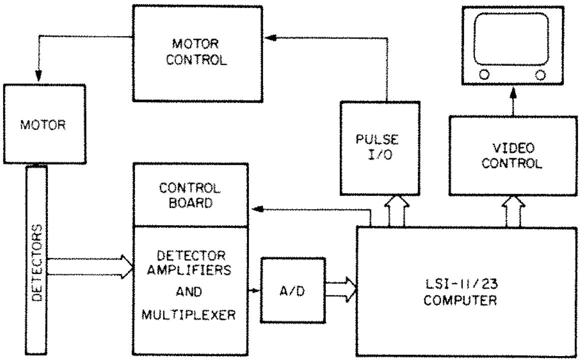

FIG. 1.

Block diagram of the electronic portal imaging system.

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*Present address: Radiation Oncology, Temple University, Philadelphia, PA 19140, USA.

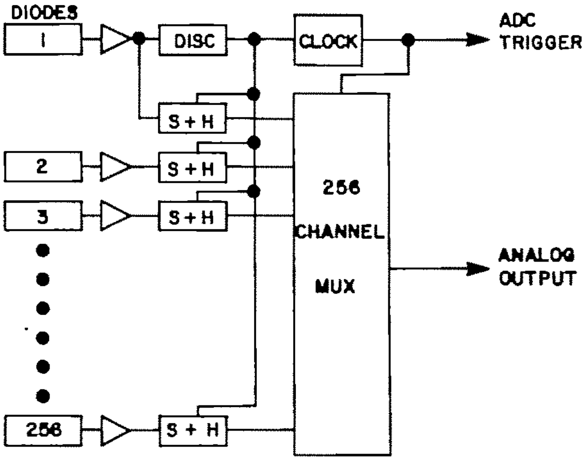

FIG. 2.

Schematic diagram of the signal processing circuitry.

top of the diodes for electronic build-up. For a 4 MV accelerator, the thickness of lead is 1.1 mm.

A schematic diagram of the signal processing circuitry is shown in Fig. 2. The cathodes of all diodes are connected to a common ground. The anode of each diode is connected to a charge amplifier having an integration time constant of 10 μs. The output voltage is proportional to the charge generated at the diode by the impinging X rays. Each diode together with its amplifier forms a channel. The output of the integrator goes through a sample-and-hold unit (S+H) to a multiplexer (MUX). The diode of the first channel of the detector array is detachable and it is mounted near the collimators of the accelerator to monitor the X-ray beam intensity. When the detected signal is above the threshold set by the discriminator (DISC) of this channel, a single signal is sent to all sample-and-hold units to start sampling the outputs of the integrators and to a clock generator to trigger the generation of 256 clock pulses. The use of sample-and-hold units ensures that signals detected in all diodes are sampled simultaneously and held at the peak voltages. The 256 clock pulses provide the switching signals for the multiplexer and also the external triggers for the analog-to-digital converter (ADC). Analog signals from the amplifiers are multiplexed and then digitised by the ADC (Data Translation Model DT2782). The ADC has a 12-bit resolution and is run in a direct memory access (DMA) burst mode with a data acquisition rate of 100 kHz using external trigger. The digitised output is fed to the computer which also does the processing of the collected data. The ADC is Q-BUS compatible and plugs directly into the LSI-11 backplane.

To scan the radiation field, the diode array is moved by the stepper motor. An open-loop control system is implemented with the computer sending the required number of pulses through a pulse output controller (ADAC Corporation Model 1604/POC) to the motor. The controller interfaces directly with the LSI-11 computer and is configured to have a pulse width of 2 ms and a pulse period of 4 ms. The step size between measurements is 2 mm, and each measurement with the 256 diodes forms a scan line. The number of scan lines and the starting position of the diode array depend on the length of the field used for the treatment. The maximum field length that can be covered is 44.8 cm in the scan plane, and this corresponds to 224 scan lines. The maximum field width is 51 cm which is the total width of the linear array of 255 diodes.

In a typical external beam radiation therapy treatment, the accelerator is run at a pulse repetition rate of about 200 pulses/s, with each pulse having a 4.5 μs duration. When the beam is turned on, the first X-ray pulse detected by the monitor diode mounted on the accelerator gantry starts the scanning process.

For on-line display on the video monitor, two graphics controller boards QRGB-GRAPH and a graphics support board QVAF-512 by Matrox Electronic Systems are used. The two QRGB-GRAPH boards, arranged in a master–slave configuration, and the QVAF-512 board are strapped to provide a 512 pixels by 512 pixels by 8 bits system, giving 256 levels of grey for each pixel. For displaying on the monitor, the signal at each diode position can be mapped to a single pixel or zoomed by a factor of two.

Computer software

The LSI-11/23 computer is run under the RT-11 operating system. For ease of programming and program maintenance, a high-level language such as FORTRAN should be used. However, because of the speed required in real-time application and of the software compatibility with the hardware supplied by a third party, it is necessary to code part of the program in assembly language (MACRO-11).

The LSI-11 is a 16-bit computer and its basic architecture provides only 16-bit addressing. It can only directly address 64K bytes or 32K words. However, the image array itself takes about 64K words. Through the use of a memory management unit, it can access larger arrays. Since the data acquisition is carried out in real time, MACRO-11 is used to address the image array for processing speed. Through its extended memory monitor, RT-11 provides a mechanism to associate a virtual address with a physical address by mapping virtual addresses to physical memory locations. In order to put a large array into the extended memory, a region large enough to store the array and a virtual address window of a size that the program can afford are created. The virtual addresses are associated with physical memory locations by mapping the windows to the regions.

The program for interfacing the ADC to the computer also requires the use of MACRO-11. A double buffering technique is used to process the incoming data: while 256 words of digitised signals are going into one buffer under DMA, the data in the other buffer are summed with the corresponding data in the image memory and written back into the image memory. The number of summations depends on the number of pulses accumulated in each channel. After receiving the data of a pre-set number of pulses, the computer sends out a signal in the form of a series of pulses to the stepper motor to move the diode array by a distance of 2 mm perpendicular to the X-ray beam and then takes another set of data from the ADC.

After the scanning has been completed, the signal level of each diode is corrected for the detection efficiency and the background noise. The signals of all the diodes in each scan line are in turn corrected for intensity fluctuations of the X-ray beam as detected by the monitor diode. The collected data are scaled to 256 levels of grey, video-reversed so that the image appears like that obtained on a radiographic film, and displayed on the video monitor with 256 pixels by 256 pixels by 8 bits. A histogram of the pixel values of the entire data is then taken and plotted below the image. By using the information of the histogram, the operator has the option of performing a simple contrast enhancement on the image by rescaling the brightness. A window of pixel values is selected according to the shape of the histogram for the region of interest. This window is again mapped linearly to 256 levels of grey. The image is then zoomed by a factor of two and redisplayed on the monitor.

Operation

The diode array, together with its drive mechanism, is mounted perpendicular to the X-ray beam. The object to be imaged is placed between the array and the X-ray source. In a typical measurement with a 100 cm isocentric machine, the diode array is 150 cm from the radiation source so that its spatial resolution in the isocentric plane is 1.3 mm.

Prior to switching on the beam, the program is run and the operator enters the information prompted by the program. Based on the information entered, the computer moves the diode array to a position just outside the radiation field. The X-ray beam is then turned on and the first beam pulse detected by the monitor diode will start the scanning and data acquisition processes. At the end of the scan, the data will be processed by the computer and the image detected by the diode array will appear on the video monitor. The image array is also stored on a floppy disk which can be viewed at a later date when the patient's case is being reviewed.

To correct for the long-term drift of the electronics, at the beginning of the day the efficiencies of the individual diodes are determined and the background noise level of each individual channel is recorded. The calibration of the diodes is done using a wide open field without any object in the X-ray beam path by giving 1000 pulses with the beam axis centred on the diode array. The collected data are then stored on the floppy disk for use in the gain normalisation of the diodes during the actual measurement. The background noise is obtained with the X-ray beam turned off, and an external pulser is used to trigger the clock generator and the sample-and-hold units.

MEASUREMENTS WITH THE IMAGING SYSTEM

Phantom experiments

The Varian Clinac 4/100 was used as the X-ray source. For the present measurements, the diode array and the moving mechanism were mounted on a cart which was placed under the treatment couch. To study the resolution of the imaging system, a series of measurements was carried out with a 25 cm × 25 cm × 7 cm polystyrene phantom having a horizontal cylindrical cavity of 1.5 cm in diameter and 14 cm in length. One-centimetre-diameter polystyrene disks with thicknesses of 1.5 mm, 3.0 mm, 4.5 mm, 6.0 mm and 7.5 mm were placed on the phantom. The thinnest disk was put at the lower right-hand side and disks of increasing thickness were arranged in a counter-clockwise pattern. Five 1.5 mm-thick disks were also placed at and around the centre of the phantom. The phantom, together with the polystyrene disks on top, was placed in the beam 100 cm from the X-ray source and the field was scanned in the manner described above. Images were generated with doses of 0.07 cGy, 0.13 cGy, 0.2 cGy, 0.27 cGy, 0.33 cGy, 0.4 cGy, 0.47 cGy and 0.53 cGy which corresponded respectively to 4, 8, 12, 16, 20, 24, 28 and 32 pulses of the X-ray beam. Each pixel in the image represented an area of 1.3 mm × 1.3 mm of the phantom. For the calculation of the attenuation of the beam, the effective energy of the X rays having a filtered bremsstrahlung spectrum of a 4 MV machine was assumed to be 1.5 MeV (White Grodstein, 1957). Using the mass–energy attenuation coefficient of 0.0557 cm^2/g for polystyrene at 1.5 MeV (Evans, 1968), the percentage contrast ratios of the disks of the five thicknesses were calculated to be 0.8%, 1.6%, 2.4%, 3.2% and 4.0%.

A humanoid phantom was used in the second measurement. The phantom consisted of a human skeleton and tissue-equivalent material. The skull, the neck and the upper thorax were imaged with an accumulation of 16 beam pulses. To see finer details of the bony skull, the phantom was moved to 80 cm from the X-ray source, giving a spatial resolution of 1 mm × 1 mm per pixel.

Patient study

The purpose of using the on-line portal imaging system is to detect errors that occur in an external beam irradiation of patients. Errors that can be detected by the system include focused blocks that were cut and/or mounted improperly, field sizes and collimator angles that were set incorrectly, portal displacement with respect to anatomic sites, and patient movement after being set up for treatment. These errors can be determined by comparing the digital image obtained for the duration of the treatment with the image of the simulation radiograph.

An initial testing of the imaging system with patients under treatment was carried out. For this initial test, only cases where the beam was directed vertically downwards were studied. The procedure for operating the system was as described above. The collected data were stored on floppy disks for detailed study. To determine the field placement errors, a direct comparison was made between the digital image and the simulation radiograph. This direct comparison was facilitated by using a graphics system consisting of a DEC VAX-11/730 computer interfaced to a Raster Technologies Model One/25 graphics display terminal and a Summagraphics Corporation Supergrid XY-digitiser.

The computer was run under the VAX/VMS operating system. The floppy disks containing the image data were written in the RT-11 format. The file transfer utility (FLX) program was used to convert the data to the Files-11 format for the VAX-11. By making use of the graphics capabilities of the Model One, the image obtained by the electronic portal imaging system was displayed on the video monitor. A program was written using the system services software of the VAX-11 to interface the digitiser to the computer. The portal and some distinct anatomic structures in the simulation radiograph were digitised and drawn as outlines which were superimposed on the portal image. The interactive graphics allowed the outlines to be magnified, shifted and rotated in the display. From the extent of the mismatch, the magnitude of the errors in the patient set-up, in the mounting of the shielding blocks and in the settings of the field size and the collimator angle could be determined.

RESULTS AND DISCUSSION

Figures 3–6 show examples of the images obtained by the system. The video images displayed on the monitor have a better quality than those shown here in the photographic reproduction. These figures were selected from three or four pictures taken with different speeds and apertures of the camera.

Samples of polystyrene phantom images are shown in Fig. 3. The eight-pulse image is at the upper left-hand corner, the 24-pulse image at the upper right-hand corner, and the 16-pulse image at the lower right-hand corner. The two areas with a darker shape on each photograph were due to the non-uniformity of the radiation field at the maximum build-up depth used in the gain calibration of the silicon diodes. The non-uniformity is an inherent beam characteristic of the Clinac 4, which has "intensity horns" of about 10% at this depth (Hansen et al, 1972). Since the calibration was done in the middle of the field with the orientation the same as that of the cylindrical cavity, the two dark spots were symmetrical about this midline. They can be removed by filtering. An image receiving 16 pulses with a filtering of 13 pixels by 13 pixels is shown at the lower left-hand corner in Fig. 3. Although the dark spots were eliminated, some edge enhancement and contrast degradation occurred in the filtering process. Because of the contrast degradation in the image, the filtering procedure was not incorporated into the system.

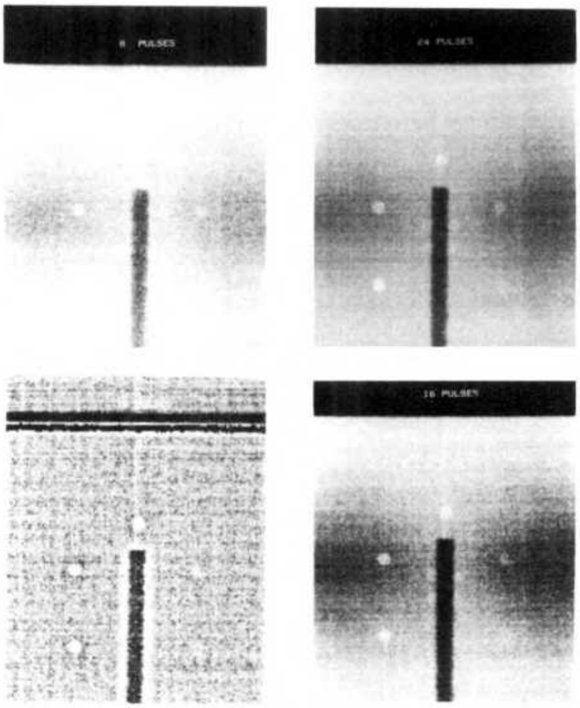

FIG. 3.

Images of the test phantom. The eight-pulse image is shown at the upper left, the 24-pulse image at the upper right, the 16-pulse image at the lower right, and the 16-pulse image with a 13 pixels by 13 pixels low-pass filter at the lower left.

As can be seen in Fig. 3, the resolution is improved with the increasing number of beam pulses accumulated. Increasing the statistics by accumulating more pulses also reduces the "graininess" of the image. The image with eight pulses shows a rather coarse-grained appearance, whereas in the image with 24 pulses the variation appears more gradual. The grainy appearance in these images was due to the fact that a very small window of pixel values was used to rescale the brightness to 256 levels of grey. The 0.8% contrast disks at the centre are distinctly visible in the 16- and 24-pulse images but only at the edge of discernibility in the eight-pulse image. The 0.8% contrast disk at the lower right is hardly distinguishable from the background, probably due to some deterioration of contrast resolution off the central position where the diodes were calibrated. The background grid pattern in the images was due to the supporting structure made of tennis racket nylon strings.

The phantom study shows that increasing the statistics improves the contrast resolution of the image.

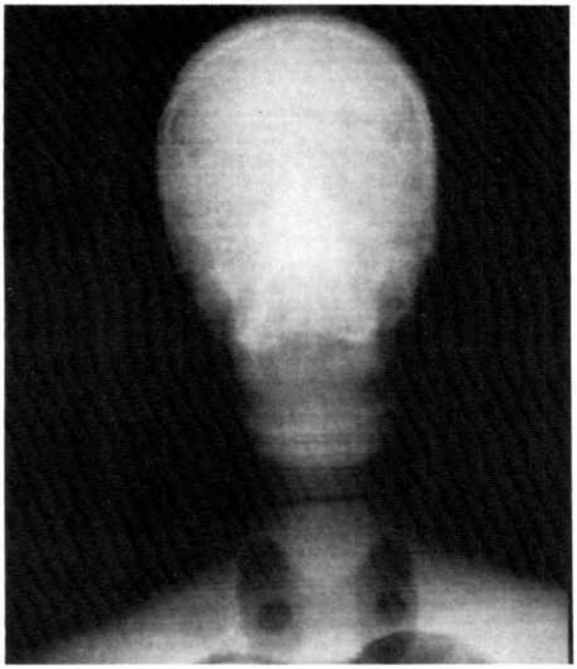

FIG. 4.

Humanoid phantom image receiving 16 pulses of X rays.

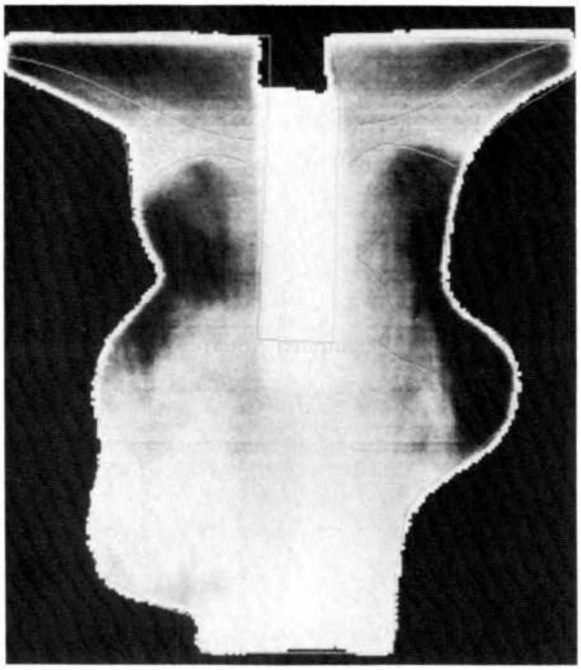

FIG. 5.

A portal image of the thoracic region of a patient.

The statistics only increase with the square root of the number of X-ray pulses. However, because the maximum time available for scanning is limited by the time actually taken in the treatment, the number of pulses used in the measurement has to be kept to the minimum that gives a reasonable resolution. With 16 pulses, there is ample time to scan a normal treatment which requires about 5000 beam bursts.

The image of the humanoid phantom is shown in Fig. 4. In this case a much wider window of pixel values was used to set the grey scale and the graininess has disappeared. In addition, the non-uniformity in the calibration has a less pronounced effect. Fine details of the bony structure are clearly visible. By changing the video display window, details of the lower jaw and neck can also be seen.

No matter how complex is the patient set-up, when the digitised outlines from the simulation radiograph are superimposed on the digital portal image, the displacement of the outline from its corresponding image can be easily determined. When the patient was accurately set up, this would be shown as an exact match in the overlaid display. Figure 5 shows an example when the set-up was not done according to the prescription. In addition to shielding blocks, a transmission block (upper central region in the portal) was used to reduce the radiation given to the spinal cord. This picture shows that the transmission block was mounted incorrectly.

Figure 6 shows another picture of digitised outlines of the shielding blocks and bony landmarks superimposed on the patient's portal image. This port includes the lower spine and part of the pelvis. The upper part of the port appears to be brighter than usual, because the radiation had to pass through the thick support of the treatment couch. Portal alignment was good except for a slight displacement of a small protrusion at the level of the second vertebral body of the lumbar spine. With the digitised outlines superimposed on the digital image, the displacement shows up distinctly. This direct comparison makes error detection easy. Such an error would be very difficult to detect if the operators were comparing two radiographs side by side. The error can be corrected by recutting the shielding blocks.

The use of an imaging system to monitor the treatment portal provides a means of detecting errors and, hence, correcting them before the treatment progresses. It will be valuable to develop a real-time monitor system which can detect errors at the beginning of and during an irradiation, so that corrective action may be taken before further irradiation proceeds.

At present the imaging system has been implemented by using the LSI-11 computer. For the study of localisation errors the outline digitising was done on the VAX-11 computer, which normally performs other functions such as treatment planning. The required data transfer for the error analysis was carried out by using floppy disks. This data communication can be improved by using a direct link, such as a local area network. For

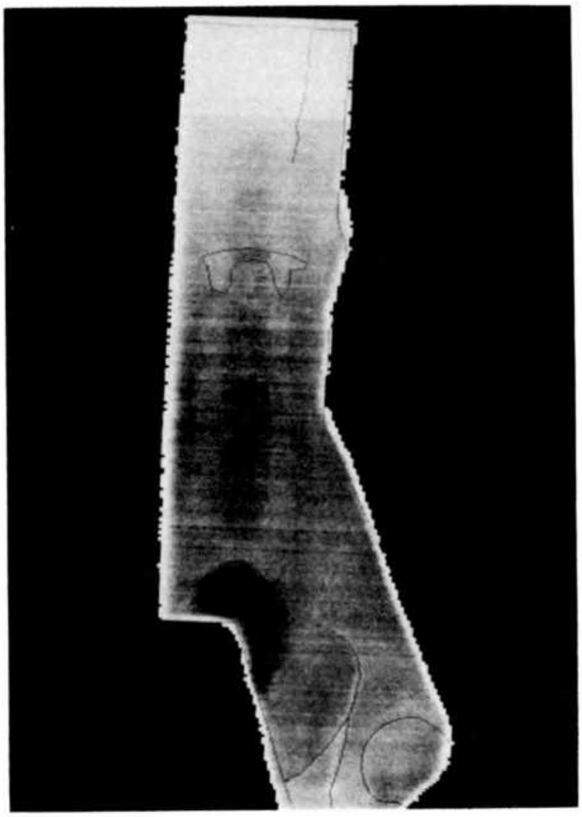

FIG. 6.

An image of a treatment portal which includes the spine and part of the pelvis.

a small radiotherapy department, however, all the components can be packaged in one computer.

As a further improvement to the system, a video digitising system can be used to obtain outlines from the simulation radiograph. By using edge-enhancement techniques and background subtraction, the outlines of anatomic sites and shielding blocks can be generated automatically. The information may then be stored on the magnetic disk to be recalled for comparison with the digital image for error detection. By using a multi-user computer, the design can support multiple portal imaging systems for all the therapy machines of the department and provide a central station for reviewing. With two monitors at the central station—one for the simulation radiograph image and another for the digitised outlines of the simulation radiograph superimposed on the digital portal image—the system will allow both direct and side-by-side comparison.

CONCLUSION

An on-line electronic portal imaging system has been developed. The image quality obtained with this system compares well with the best conventional verification radiographs. In contrast to verification radiographs, digital data can be manipulated directly by using digital image enhancement techniques to give the optimum image. In addition, the "brightness" and "contrast" controls of the monitor can be adjusted to highlight details in the region of interest. Furthermore, direct comparison by superimposing digitised outlines from the simulation radiograph on the portal image is far superior to comparing two radiographs of different contrasts and magnifications side by side.

The advantages of this on-line imaging system are many. The display on the video monitor will reveal the error in the patient set-up and make the machine operators more conscious in this procedure. To those who review the treatment, this will allow them to take the corrective action when it is needed. Besides, the system keeps a record of all the portals of the treatments that the patient has been given. Digital image data can be stored on a magnetic disk. Data retrieval is fast and simple. For archiving, data can be transferred from disks to other mass storage media such as magnetic tapes.

Attempts have been made to digitise the verification radiograph (Leong, 1984; Meertens, 1985). However, because of the extra cost of the X-ray films, this indirect procedure is not as cost-effective as the system presented here.

All these features make on-line portal imaging for external beam radiotherapy far superior to the conventional verification radiographing procedure. The use of such a system to monitor the treatment portals of patients routinely will help towards improvement in technical precision in the delivery of external beam radiation therapy.

ACKNOWLEDGMENTS

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REFERENCES

BYHARDT, R. W., COX, J. D., HORNBURG, A. & LIERMANN, G., 1978. Weekly localization films and detection of field placement errors. *International Journal of Radiation Oncology, Biology, Physics*, *4*, 881–887.

EVANS, R. D., 1968. X-ray and γ-ray interactions. In *Radiation Dosimetry*. Ed. by F. H. Attix & W. C. Roesch (Academic Press, New York), Vol. I, p. 121.

HANSEN, H. H., CONNOR, W. G., DOPPKE, K. & BOONE, M. M. L., 1972. A new field flattening filter for the Clinac 4. *Radiology*, *103*. 443–446.

KELSEY, C. A., LANE, R. G. & CONNER, W. G., 1972. Measurement of patient movement during radiation therapy. *Radiology*, *103*, 697–698.

LEONG, J., 1984. A digital image processing system for high energy x-ray portal images. *Physics in Medicine and Biology*, *29*, 1527–1535.

MARKS, J. E., HAUS, A. G., SUTTON, H. G. & GRIEM, M. L., 1974. Localization error in the radiotherapy of Hodgkin's disease and malignant lymphoma with extended mantle fields. *Cancer, 34*, 83–90.

——1976. The value of frequent treatment verification films in reducing localization error in the irradiation of complex fields. *Cancer, 37*, 2755–2761.

Meertens, H., 1985. Digital processing of high energy photon beam images. *Medical Physics, 12*, 111–113.

Norwood, H. M. & Stubbs, B., 1984. Patient movements during radiotherapy. *British Journal of Radiology, 57*, 155–158.

Taborsky, S. C., Lam, W. C., Sterner, R. E. & Skarda, G. M., 1982. Digital imaging for radiation therapy verification. *Optical Engineering, 21*, 888–893.

White Grodstein, G., 1957. *X-ray Attenuation Coefficients from 10 keV to 100 MeV*. US National Bureau of Standards Circular No. 583.

Book reviews

Information Processing in Medical Imaging. By S. L. Bacharach, pp. 555, 1986 (Martinus Nijhoff, Dordrecht, The Netherlands), £65.25
ISBN 0–89838–787–6

This is a collection of 38 papers presented to the biennial conference on Information Processing in Medical Imaging, held in June 1985 in Washington DC. The Conference is a brave and, apparently, successful attempt to bring together scientists working in different areas of application to explore common ground in techniques of processing and analysis. Sixteen contributions cover applications in nuclear medicine, six in X radiology, four in magnetic resonance imaging and four in other specific medical imaging modalities. Eight papers are on aspects of image processing, theory or display independent of physical technique.

The book begins with impressive general papers on morphology, shape analysis and human visual signal detection theory Several papers deal with the increasingly sophisticated techniques of pattern recognition and the automatic description and analysis of images Multiresolution segmentation procedures receive significant attention with a principal aim being to achieve tissue characterisation from magnetic resonance images. Other papers deal with the development of expert systems and databases, simulation and modelling of imaging processes, computer languages, tomographic reconstruction, factor analysis for dynamic studies, Fourier analysis, correlation and combination of images and data compression techniques A few contributions deal with specific novel instrumentation: ionography, ophthalmological photography, infra-red tissue transillumination and electrical impedance mapping.

There is no classification of the contents, no subject index and no author index Although described as a "Conference Proceedings", there is no record of discussions. While the subject matter is certainly diverse, there is no suggestion that it should be considered comprehensive or balanced. The book's sole purpose is to publish 38 papers and it will be used as a source of reference like any scientific journal.

R. A SHIELDS

Principles of Nuclear Radiation Detection. By G. G. Eichholz and J. W. Poston, pp. xix+379, 1985 (Lewis, Publishers Inc., Michigan), £36.76 (hardback).
And the accompanying *Laboratory Manual.* pp. viii+171+appendix, £15 60 (paperback).
ISBN 01–87371–062–2

The authors have capitalised on their extensive experience of radiation detection techniques by producing a comprehensive textbook which admirably links physics theory with technological practice. In the 15 years since the last general textbooks were published (and to which the authors refer) there have been many significant developments, the inclusion of which, albeit to a varying degree, has brought the subject up to date. Whereas there is extensive coverage of modern semiconductor detectors, the treatment of the medical scintillation camera is almost archaic and the references to recent literature are scant.

This book is primarily for the student, probably at M.Sc. level The design is logical (a chapter for each class of detector), the style is clear, and each chapter concludes with a useful collection of questions for the reader The book is well illustrated, but in the reviewer's copy the quality of printing of some of the diagrams is not good.

The *Laboratory Manual* is a companion volume which reproduces introductory notes, procedures and discussion topics on some 34 practical experiments. The design follows the same logical sequence as the main textbook and it is amply cross-referenced. Here is a ready-made practical course in nuclear radiation detection which should be of considerable value to both student and teacher. Both volumes are highly recommended

R. A. SHIELDS

1986, *The British Journal of Radiology*, 59, 1015–1022 OCTOBER 1986

Cell kinetics of normal and perturbed populations measured by incorporation of bromodeoxyuridine and flow cytometry

By N. J. McNally and G. D. Wilson

Cancer Research Campaign Gray Laboratory, Mount Vernon Hospital, Northwood, Middlesex HA6 2RN

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ABSTRACT

Bromodeoxyuridine (BrdU) incorporation and flow cytometry have been used to measure the kinetics of V79 cells growing at different temperatures *in vitro* and cells of the murine Sa F tumour growing *in vivo*. By simultaneously measuring total DNA content and BrdU incorporation in individual cells at different times after pulse labelling with BrdU, it is a simple procedure to quantify the movement of cells through the cell cycle. The method has the advantage of speed (2×10^4 or more cells are analysed within a day or so of the experiment) and the ability to analyse the results in different ways. A G2 block in tumour cell progression *in vivo* is readily detected after a dose as low as 2 Gy. The neutron relative biological effectiveness for this G2 block is probably larger than that for tumour growth delay

Measurements of tumour cell kinetics have in the past relied on autoradiographic methods to detect the uptake of radioactive precursors into the DNA of actively proliferating cells. The "per cent labelled mitoses" curve measuring the movement of cells labelled with tritiated thymidine through mitosis has been used extensively to estimate the phases of the cell cycle (see Cleaver (1967) and Steel (1977) for extensive reviews). Such autoradiographic techniques can be extremely laborious and time-consuming and can lack precision and resolution when applied to perturbed populations, or those in which the mitotic index is low and only quite a small fraction of the cells are dividing.

As a consequence of the limitations of the autoradiographic techniques, attempts to use cell population kinetic information as an aid in cancer therapy have been somewhat disappointing. Doubts have been expressed as to whether experimental laboratory studies can ever be of use as a guide to the application of chemotherapy to human cancer, in spite of the importance of cell kinetics in determining chemotherapeutic response (Hall, 1971). Others have taken a more optimistic view, although clearly recognising the limitations of the autoradiographic techniques (*e.g.* van Putten, 1974). In relation to the radiation response of tumours, cell kinetics has been thought of as even less important. However, interest in accelerated fractionation in which the overall treatment time is shortened to 3 weeks or less, as a method to increase the therapeutic gain, has emphasised the need to measure kinetic parameters in human tumours, in particular the potential doubling time (Steel, 1977). Tumours with a short potential doubling time of 5 days or less may undergo significant repopulation during conventional fractionated radiotherapy and would be candidates for accelerated fractionation (Thames et al, 1983; Fowler, 1986). A knowledge of cell kinetics could also be important in the clinical application of high linear energy transfer (LET) radiation; for instance, differences in cell kinetics between rapidly dividing tumour cells and slowly dividing cells of the late responding, dose limiting normal tissues could lead to a "kinetic gain factor" due to differential reassortment through the cell cycle, in favour of high LET radiation, at least as large as the gain resulting from the reduced oxygen enhancement ratio (Withers & Peters, 1980).

In order to predict which tumours might benefit from accelerated fractionation by virtue of a short potential doubling time, or from high LET radiation due to a significant kinetic gain factor, methods are needed to estimate rapidly the kinetic characteristic of individual tumours, or those of a given type. Experimental studies have been hindered by the lack of suitable rapid methods for measuring tumour cell kinetic parameters and their perturbation by radiation doses of a few grays. Autoradiographic methods have been used to measure such changes 1 day after 6 Gy to a solid mouse tumour (Szczepanski & Trott, 1975), and 2 days after 6 5 Gy to an ascites tumour (Frindel et al, 1970), but the results were not obtained for several weeks after the experiment because of the exposure time for the autoradiographs.

The development of a monoclonal antibody to bromodeoxyuridine (BrdU) incorporated into DNA and of suitable flow cytometric methods to measure this incorporation simultaneously with the total DNA content (Gratzner, 1982, Dolbeare et al, 1983) provide the opportunity to measure cell kinetics rapidly and quantitatively on individual tumours. The method may be applicable to measurements of some parameters of human tumour cell kinetics, since BrdU is not radioactive and is relatively non-toxic in humans (see, for example, Wilson et al, 1985).

In this paper we present our initial studies on the cell kinetics of a transplantable mouse tumour, and their perturbation by radiation. We also present some results on cells in culture and demonstrate that the BrdU technique can detect changes in tumour cell kinetics after quite small doses of radiation and in particular can provide the information within a day of treating the tumour.

MATERIALS AND METHODS

Cultured cells

V79 379A Chinese hamster fibroblasts were grown in spinner culture in minimum essential medium modified for suspension culture, plus 7.5% fetal calf serum and antibiotics. For the experiments, cells were grown in temperature-controlled water baths maintained at either 37°C or 32°C. Bromodeoxyuridine freshly dissolved in medium was added to cultures in logarithmic growth to give a final concentration of 10 μM. After 1 h the cells were washed twice with pre-warmed medium to remove the BrdU and then returned to the water baths at the appropriate temperatures. Samples were taken at various times thereafter, resuspended in 1 ml of phosphate buffered saline (PBS) and added to 70% absolute alcohol to fix the cells before staining for flow cytometry.

Tumours

The Sa F tumour growing in CBA mice was transplanted on to the back of mice and irradiated when it had reached a diameter of about 6 cm. The methods for transplanting and irradiating have been described before (McNally et al, 1979). The tumours were irradiated in unanaesthetised mice either with 250 kVp X rays or with neutrons generated by accelerating 4 MV deuterons onto a beryllium target in the Gray Laboratory Van de Graaff accelerator, as described before (McNally et al, 1982). For kinetic studies, mice were injected intraperitoneally with 100 mg/kg BrdU in PBS immediately before their tumours were irradiated. They were then sacrificed at various times after irradiation, the tumours were excised and single-cell suspensions were prepared as previously described (McNally et al, 1979). The cells were then washed and fixed in 70% absolute alcohol at a concentration of 1×10^6 per ml. The half-life of BrdU in rodent blood is short, so that a single intraperitoneal injection results in "pulse labelling" of the tumour cells over a period of, at most, about 15 min (Kriss & Revesz, 1962).

Tumour growth delay was measured by constructing tumour growth curves for each mouse and measuring the time to grow to twice the treatment volume. Six to eight mice were used for each dose group, and their times to regrow to the appropriate size were averaged and the standard error calculated. The growth delay was then calculated as the difference between this time and the corresponding time for unirradiated mice.

Bromodeoxyuridine staining and flow cytometry

Cells were stained for their BrdU and DNA content using a modification of Dolbeare's method (Dolbeare et al, 1983) as described in detail by Wilson et al (1985). The cells were then usually left overnight before assaying for BrdU and DNA content. Fluorescence was determined using an Ortho Systems 50 Cytofluorograph and dedicated Ortho 2150 computer. Excitation was at 488 nm from a 5 W argon-ion laser operating at 100–200 mW. Fluorescent light was collected at 90° to the incident beam. Following passage through a dichroic lens to deflect exciting light, green fluorescence (BrdU content) was collected between 510 nm and 560 nm and red (DNA content) between 620 nm and 740 nm. Data were collected in list mode, gating on the red peak versus area signal to exclude doublets. At least 2×10^4 cells were analysed.

RESULTS

V79 cells

Figure 1 shows bivariate distributions (expressed as contour plots) of BrdU content (y axis) versus DNA content (x axis) for V79 cells grown at 37°C (left-hand column) or 32°C (right-hand column) and sampled at various times after BrdU labelling. The population doubling time was increased from 10 h at 37°C to about 36 h at 32°C and this is clearly reflected in these distributions.

For cells at 37°C at 1 h, *i.e.* immediately after removing the BrdU, the S-phase cells are clearly identified by their green fluorescence. The G1 and G2 population (at about channel numbers 19 and 40) do not show significant green fluorescence. (Staining of cells that had not been given BrdU gave no green fluorescence above channel 10 on the y axis, data not shown). By 6 h the majority of the BrdU-labelled cells at 37°C had moved out of S, through G2 and into G1. The cells with the S-phase DNA content showed minimal green fluorescence. At 9 h none of the G2 cells contained BrdU and the bulk of the initially labelled population had re-entered the S-phase. Progression through the cell cycle was much slower for cells at 32°C (right-hand column of Fig. 1). At 9 h only a few of the initially BrdU-labelled cells had progressed to G1, the majority of them being in late S and G2. Even by 12 h a significant proportion of them were still in late S and G2. The quantification of these differences is presented in the discussion.

Tumours

Sa F tumours were either sham irradiated or irradiated with either 2 Gy, 5 Gy or 10 Gy of X rays or 3 Gy of neutrons immediately after injecting the BrdU. The respective times to grow to twice the initial diameter (eight times the volume) are shown in Table I; 10 Gy of X rays gave the same tumour growth delay as 3 Gy neutrons.

Figure 2 shows the DNA profile of the Sa F tumour together with a bivariate BrdU versus DNA profile for a tumour that had not received BrdU. This demonstrates that there is virtually no non-specific staining using the monoclonal antibody, and that it is reasonable to regard fluorescence above channel 15 on

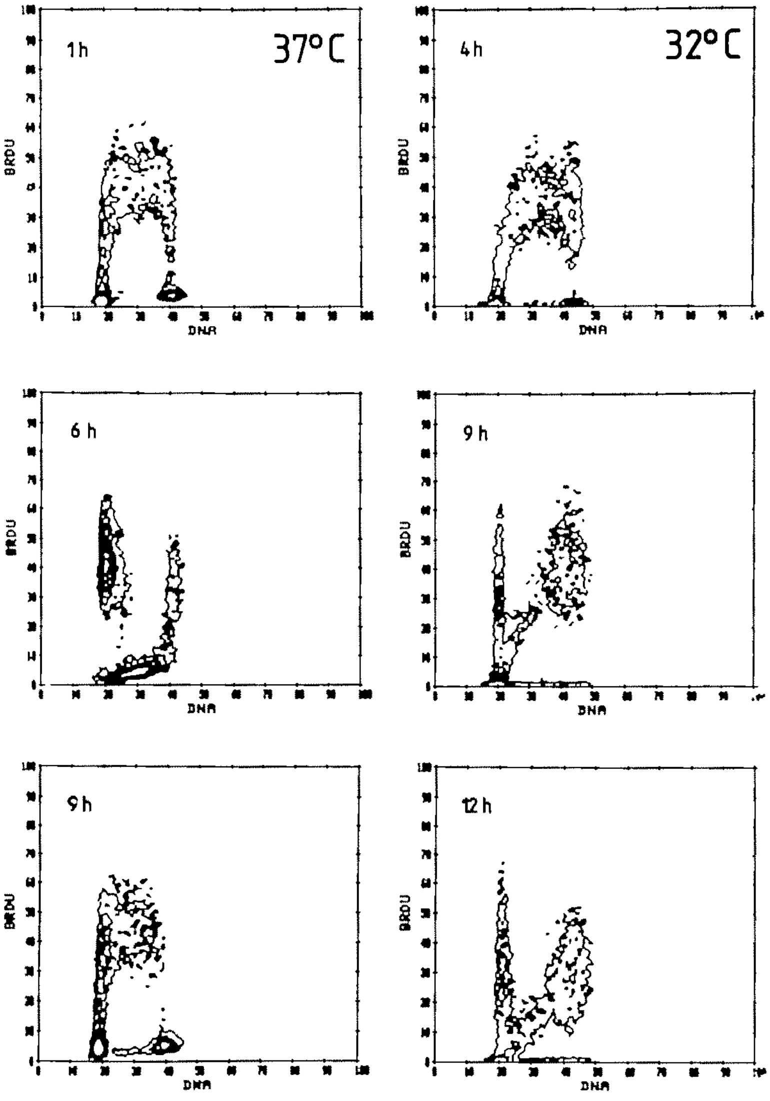

FIG. 1

Bivariate contour plots of BrdU content (ordinate) versus DNA content (abscissae) for V79 cells growing at 37°C (left-hand column) or 32°C (right-hand column). At least 2×10^4 cells were analysed for each time point in this and subsequent bivariate plots.

TABLE I

TIME TO GROW TO TWICE TREATMENT DIAMETER

Dose	Time to grow to twice treatment diameter (days ± standard error)
0	4.7 (3.4–5.6)
*	
5 Gy X rays	6.4 (5.8–6.8)
10 Gy X rays	8.6 (8–9.2)
3 Gy neutrons	8.8 (8.2–9.3)

*The value for tumours exposed to 2 Gy X rays was similar to the control value

the *y* axis as indicative of BrdU uptake. The DNA profile (Fig. 2B) shows that the tumour is tetraploid.

Bivariate distributions of DNA versus BrdU content for control tumours and those irradiated with 5 Gy of X rays are shown in Fig. 3. The left-hand column shows distributions for unirradiated tumours excised 1 h, 6 h and 10 h after injecting the BrdU. The right-hand column shows distributions for irradiated tumours excised at 6 h, 10 h and 16 h. At 1 h, the distributions were similar for all groups (irradiated and unirradiated). The G1 "normal" cells are seen at about channel 15 in all figures. As the 1 h panel shows, few diploid S-phase cells have taken up BrdU, *i.e.* were undergoing DNA synthesis, implying that this is a

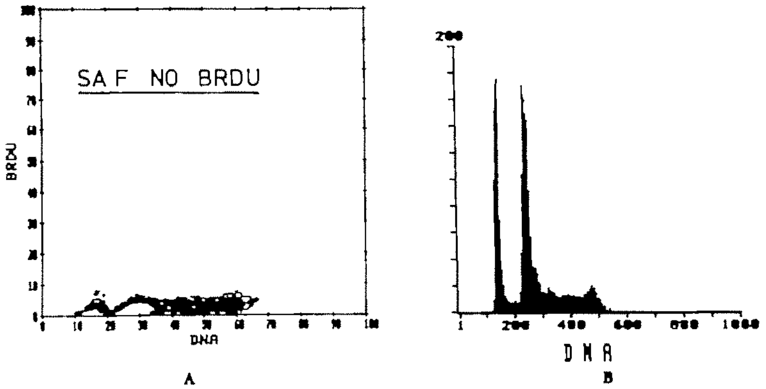

FIG. 2.

(A) Bivariate contour plot of BrdU content versus DNA content and (B) DNA profile for cells from a Sa F tumour that had not received BrdU (non-specific staining).

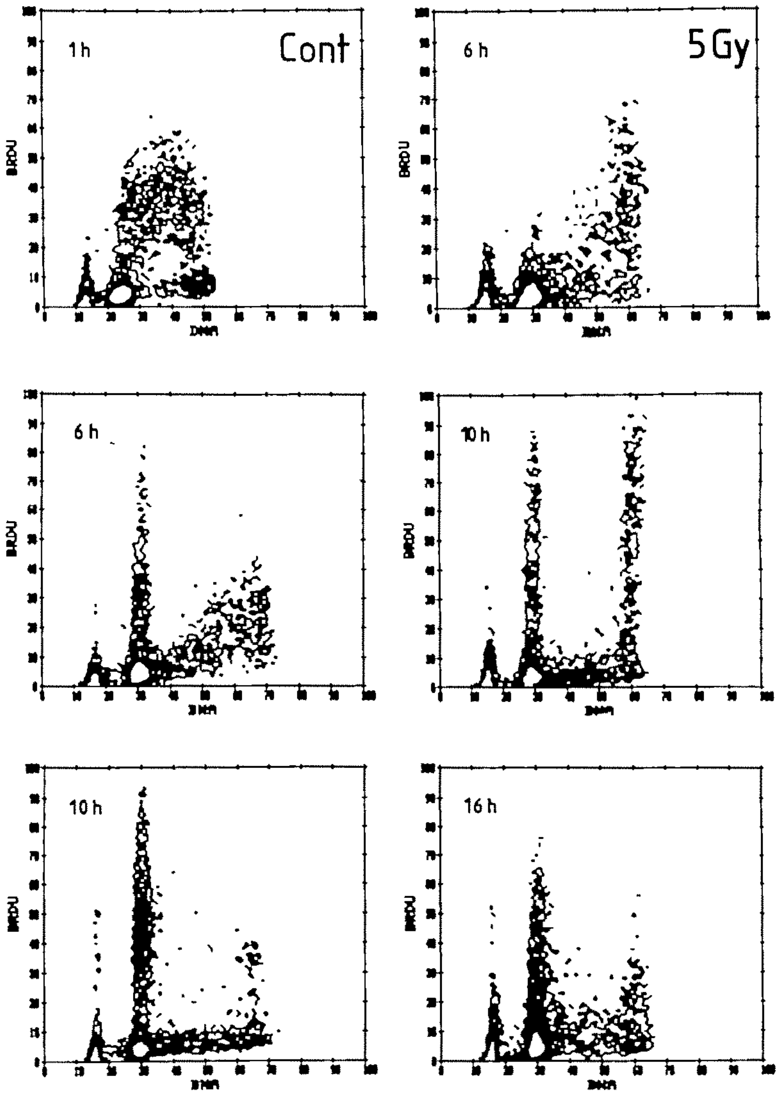

FIG 3

Bivariate contour plots of BrdU content (ordinate) versus DNA content (abscissae) for Sa F tumour cells either from unirradiated tumours (left-hand column) or tumours exposed to 5 Gy X rays (right-hand column).

slowly or non-cycling population. In contrast, about 30% of the cells between channels 20 and 50 (x axis) (*i.e.* the tetraploid tumour cells) have significant green fluorescence, implying uptake of BrdU. By 6 h, these cells in the control tumours have progressed through the S-phase and some have progressed through G2 and into G1. By 10 h the bulk of the initially labelled cells has moved from S into G1, with virtually none of the cells in S showing significant green fluorescence since they represent cells that were initially in G1 and G2. In contrast, after 5 Gy of X rays, cells progressed more slowly through the cell cycle. At 6 h (right-hand column, Fig. 3) few initially labelled cells have moved into G1. At 10 h there are still BrdU-labelled cells in G2 (contrast with 10 h control) and even at 16 h there are cells that were initially in S that have not moved out of G2 and into G1.

This radiation-induced G2 block is even more evident for tumours irradiated with 10 Gy of X rays or 3 Gy neutrons. Bivariate distributions for the cells of these tumours are shown in Fig. 4. By 10 h, for instance, few BrdU-labelled cells had entered G1 (contrast with the unirradiated tumours in Fig. 3). Even at 16 h a significant fraction of BrdU-labelled cells were still held up in the G2 block, particularly after 3 Gy neutrons (bottom panel on right-hand side), suggesting that after the neutron dose, the G2 block was more extensive than after 10 Gy X rays.

DISCUSSION

An advantage of the BrdU technique over conventional autoradiography is that there are different ways of analysing the results, using the computer facilities of the flow cytometer. We have analysed the movement of

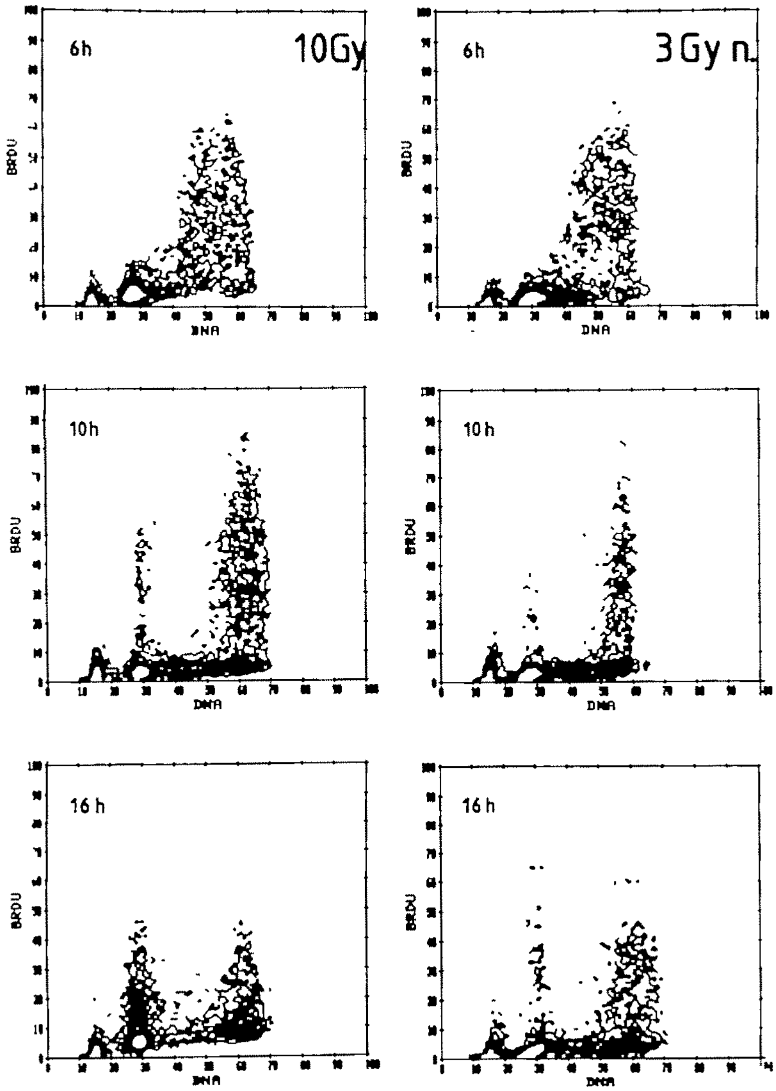

FIG. 4.

As for Fig 3 except that the left-hand column is for tumours exposed to 10 Gy X rays and the right-hand column is for tumours exposed to 3 Gy neutrons

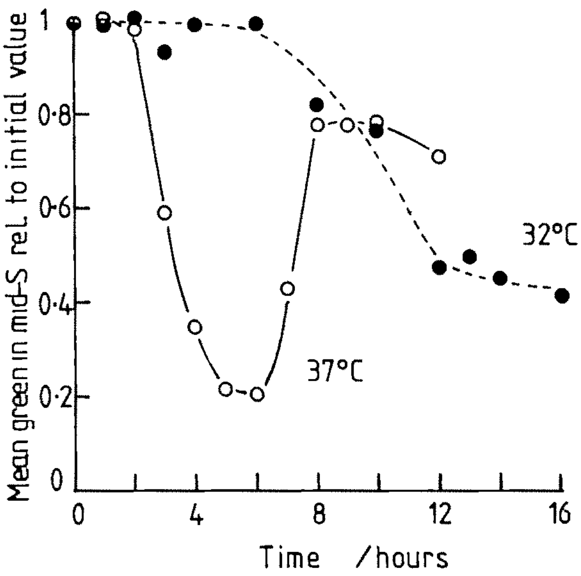

FIG. 5

Mean green fluorescence in mid-S (BrdU content) relative to the value at 1 h for V79 cells grown at 37°C or 32°C, as a function of time after labelling with BrdU.

cells through the cell cycle in two ways. First, we have calculated the mean BrdU content of cells in mid-S as a function of time, and, second, we have measured the entry of BrdU-labelled cells into G1.

Figure 5 shows a plot of the mean green fluorescence in mid-S as a function of time, relative to the value at 1 h, for V79 cells growing at 37°C and 32°C. The respective population doubling times were 10 h and approximately 36 h. Theoretically, the mean green fluorescence in mid-S should stay at its maximum value for a period equal to half T_s (the duration of the S-phase), then fall and remain low for a period equal to the cell cycle time, T_c, minus T_s and then rise again. In practice, because of the spread in values of the cell cycle parameters in the population, the curve may not be well defined. As Fig. 5 shows, the curve for V79 cells growing in culture at 37°C is quite well defined. Measuring to the midpoint of the maximum and minimum values for the green fluorescence, 0.6, $T_s/2$ is estimated to be about 3 h, and T_c-T_s to be about 4.5 h. These give a value for T_c of 10.5 h, close to the measured population doubling time of 10 h. The curve for cells at 32°C is much more spread out. Over the 16 h period in which it was measured, it is evident that T_s had lengthened considerably, by a factor of at least three, reflecting the greater than threefold increase in the population doubling time.

The curves shown in Fig. 5 are analogous to labelled mitoses curves using autoradiography. The cells synthesising DNA at a given instant are labelled (either with BrdU or tritiated thymidine), a "window" is set (mid-S or mitosis), and the movement of the labelled cells through this window is monitored. The advantage of the BrdU technique is that there is no delay for development of autoradiographs or for scoring in the microscope, and large numbers of cells are analysed for each datum point (at least 2×10^4).

Similar plots of mean green fluorescence in mid-S relative to the 1 h value are shown for the tumours in Fig. 6A. For times greater than 18 h after injecting the BrdU, the resulting bivariate distribution of BrdU versus DNA content for irradiated tumours did not show clear changes with time. This reflects the imprecision of the method at later times due to dispersion in cell cycle times, such as is seen with per cent labelled mitoses (PLM) curves in autoradiography. The curve for unirradiated cells fell to a minimum of about 40% of the initial value, and gave approximate cell cycle parameters $T_s = 10$ h, $T_c = 21$ h. For comparison, Figs 6B and 6C show data from PLM curves for the same tumour obtained by Begg (1975). Figure 6B shows the PLM curve using tritiated thymidine and autoradiography for the Sa F tumour and Fig. 6C shows the distribution of cell cycle times calculated according to the method of Steel et al (1966) from the measured PLM curve. Comparing Figs 6A and 6B, the precision of the BrdU technique is at least as good as that of the PLM method. The estimate of T_c from Fig. 6A, of 21 h, is well within the distribution shown in Fig. 6C.

Apart from the advantages of speed and ease of analysis relative to autoradiographic methods, the BrdU technique has the added advantage that the data can be analysed in different ways depending on the information required. In order to try and quantify the extent of the G2 block induced by radiation in the Sa F tumour, we have measured the entry of BrdU-labelled cells into G1. Such a plot is shown in Fig. 7 in which the proportion of BrdU-labelled cells in G1 as a fraction of the total population is plotted as a function of time. For an unperturbed population this should initially be zero if there is no overlap in the DNA contents of G1 and S-phase cells (in practice this is not the case). It should then start to rise after a time equal to T_{G2+M}, so that any G2 block should give a delay in the time that this parameter increases. As Fig. 7 shows, the G2 block is very easily visualised by this plot and is measured as the displacement in the rise of the curve for treated cells relative to the control curve. Thus 2 Gy of X rays gave a G2 block of about 3 h, 5 Gy gave a G2 block of about 4 h, 10 Gy gave a block of about 8 h and 3 Gy neutrons gave a block of at least 12 h. Since 3 Gy neutrons and 10 Gy X rays gave the same tumour growth delay (Table I), this implies that the neutron relative biological effectiveness for division delay as reflected by the G2 block is much higher than that for growth delay which, much more directly, reflects cell kill. Figure 7 also shows the sensitivity of the technique. The G2 block after 2 Gy is easily measured.

One of the most detailed studies of post-irradiation

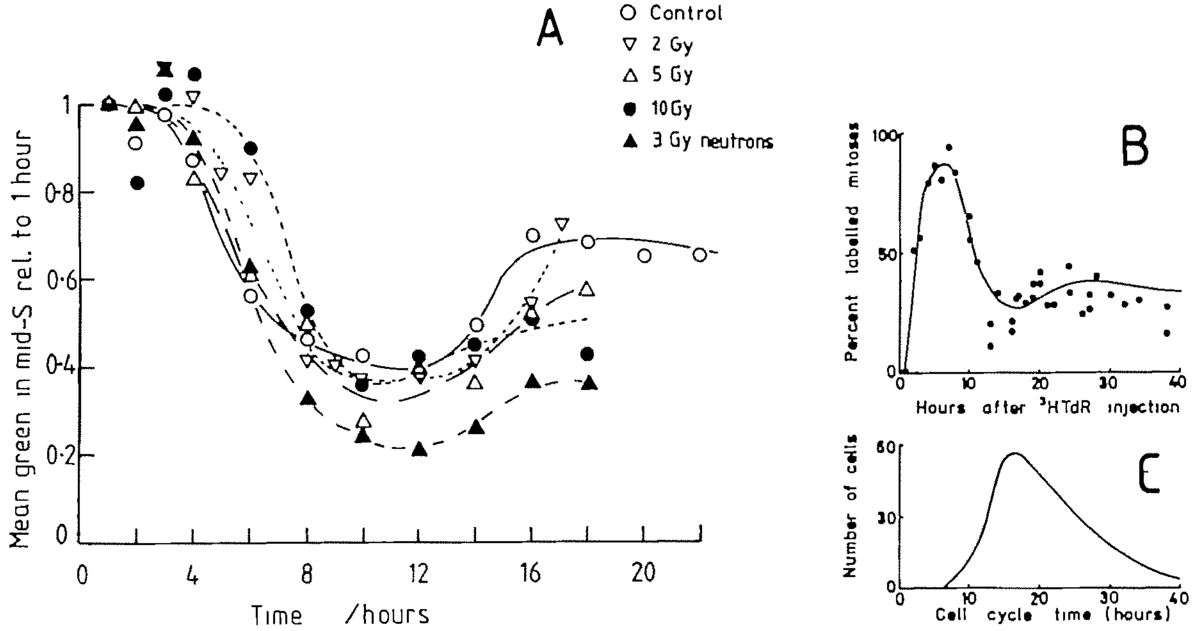

FIG. 6.

(A) Mean green fluorescence in mid-S (BrdU content) relative to initial value for cells from Sa F tumours excised at various times after irradiation with 0,2,5,10 Gy X rays or 3 Gy neutrons. Each point is for one tumour The lines were fitted by eye. The zero dose values are typical of what has been obtained in two other experiments. (B) Per cent labelled mitoses curves for the Sa F tumour (taken from Begg, 1975) (C) Distribution of cell cycle times calculated from the PLM curve (Begg, 1975).

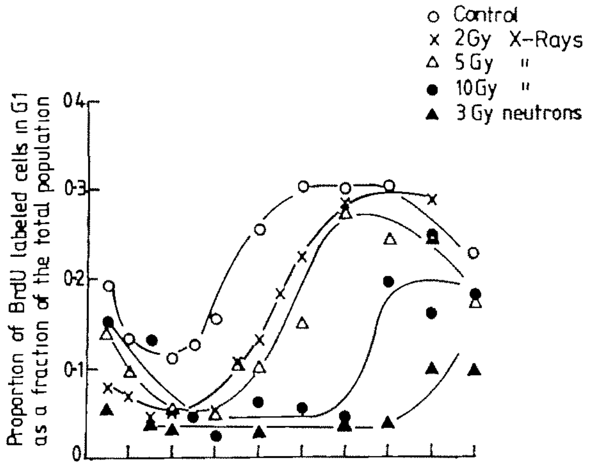

FIG. 7.

Proportion of BrdU labelled cells from Sa F tumours in G1 expressed as a fraction of the total population, as a function of time after irradiation. Each point is for a single tumour and the lines have been fitted by eye. This plot measures the entry of initially "pulsed labelled" S-phase cells into G1

proliferation kinetics in tumours was by Szczepanski and Trott (1975) using a mouse adenocarcinoma and autoradiography. This was a rapidly growing tumour with an exceptionally short cell cycle time of 13.6 h (median value). They measured the cell kinetics using the PLM technique at various times from 1 day to 8 days after doses of 6 Gy or 12 Gy. They also measured the mitotic and labelling indices. Six gray induced a G2 block such that 12 h after irradiation over 80% of proliferating cells had accumulated in G2. This contrasts with our results which show that cells that had been labelled with BrdU immediately before irradiation had entered G1 by 8 h to 10 h after 5 Gy. This difference probably reflects the differing kinetic characteristics of the two tumours. Frindel et al (1970) measured the cell kinetics of the NTC 2472 ascites tumour in mice 20 h and 2 days after a dose of 2.5 Gy and observed a lengthening of the cell cycle with little change in the duration of G2, most of the increase being due to increases in T_s at 20 h and T_{G1} at 2 days.

The changes in tumour cell kinetics that we have observed are qualitatively similar to those observed by others using autoradiographic techniques (see Steel (1977) for a review). The advantages of the BrdU technique are that it is rapid and sensitive. We were able to detect a G2 block in the Sa F tumour *in vivo* after a dose as small as 2 Gy (Fig. 7). Pallavicini et al (1985) have shown that the BrdU technique is equally sensitive in measuring perturbations in tumour cell kinetics *in vivo* after drug treatment. BrdU has been administered to patients. It is relatively non-toxic and human tumour labelling with BrdU can be detected (Hoshino et al, 1985; Wilson et al, 1985). It should now be possible to obtain *in vivo* tumour cell kinetic information of clinical relevance, both in experimental tumours and in man. For instance, it should be possible to estimate the potential doubling time in human tumours from a single biopsy following injection of BrdU (Begg et al, 1985), and to correlate its value and the tumour labelling index with clinical results.

In conclusion, the BrdU technique we have described is rapid, quantitative and sensitive. By acquiring data in list mode it is possible to re-analyse the results in different ways after the experiment is completed. The technique is applicable to the study of normal tissue cell kinetics as well as tumours and is already being applied to the study of human tumour cell kinetics.

Acknowledgments

We thank Professor J. F. Fowler for helpful discussions and Alex Lewis and Jenny de Ronde for expert technical help. We also thank Brian Hall and his team for providing the neutrons. We thank the Cancer Research Campaign for the entire financial support.

REFERENCES

Begg, A. C., 1975. Ph D. Thesis, University of London.

Begg, A. C., McNally, N J., Shrieve, D. C. & Karcher, H., 1985. A method to measure the duration of DNA synthesis and the potential doubling time from a single sample. *Cytometry, 6*, 620–626.

Cleaver, J. E., 1967 Thymidine metabolism and cell kinetics. *Frontiers of Biology*. (North-Holland, Amsterdam) Vol. 6.

Dolbeare, F A., Gratzner, H. G., Pallavicini, M. G. & Gray, J W., 1983. Flow cytometric measurement of total DNA content and incorporated bromodeoxyuridine. *Proceedings of the National Academy of Sciences, 80*, 5573–5577.

Fowler, J. F., 1986. Potential for increasing the differential response between tumours and normal tissues: can proliferation rate be used? *Proceedings of 3rd International Rome Symposium on Tumour Radiosensitivity*, in press.

Frindel, E., Vassort, F. & Tubiana, M., 1970. Effects of irradiation on the cell cycle of an experimental ascites tumour of the mouse. *International Journal of Radiation Biology, 17*, 329–337.

Gratzner, H. G., 1982. Monoclonal antibody to 5-bromo- and 5-iododeoxyuridine. A new reagent for detection of DNA replication. *Science, 218*, 474–475.

Hall, T. C, 1971. Limited role of cell kinetics in clinical cancer chemotherapy. *National Cancer Institute Monograph, 34*, 15–17.

Hoshino, T., Nagashima, T., Murovic, J., Levin, E. M., Levin, V.-A. & Rupp, S. M., 1985. Cell kinetic studies of *in situ* human brain tumours with bromodeoxyuridine. *Cytometry, 6*, 627–632.

Kriss, J. P & Revesz, L., 1962. The distribution and fate of bromodeoxyuridine and bromodeoxycytidine in the mouse and rat. *Cancer Research, 22*, 254–265

McNally, N. J., George, K. C. & de Ronde, J., 1979. Recovery from sublethal damage by acutely hypoxic tumour cells *in vivo* and *in vitro*. *British Journal of Radiology, 52*, 642–649

McNally, N. J., Maughan, R. L., de Ronde, J. & Roper, M. J., 1982. Measurements of some radiological and physical properties of neutrons produced by a 4 MV Van de Graaff accelerator. *Radiation Research, 89*, 227–237.

Pallavicini, M G., Summers, L. J., Dolbeare, F. D. & Gray, J. W., 1985. Cytokinetic properties of asynchronous and cytosine arabinoside perturbed murine tumours measured by simultaneous bromodeoxyuridine/DNA analysis. *Cytometry, 6*, 602–610.

Putten, L. van, 1974. Are cell kinetic data relevant for the design of tumour chemotherapy schedules? *Cell and Tissue Kinetics, 7*, 493–504

Steel, G. G., 1977. *Growth Kinetics of Tumours* (Clarendon Press, Oxford).

Steel, G. G, Adams, K. & Barrett, J. C., 1966. Analysis of the cell population kinetics of transplanted tumours of widely-differing growth rate. *British Journal of Cancer, 20*, 784–800.

Szczepanski, L. & Trott, K.-R., 1975. Post-irradiation proliferation kinetics of a serially-transplanted murine adenocarcinoma. *British Journal of Radiology, 48*, 200–208.

Thames, H. D., Peters, L. J., Withers, H. R. & Fletcher, G. H, 1983. Accelerated fractionation vs hyperfractionation: rationale for several treatments per day. *International Journal of Radiation Oncology, Biology, Physics, 9*, 127–138.

Wilson, G D., McNally, N. J., Dunphy, E, Karcher, H. & Pfragner, R., 1985. The labelling index of human and mouse tumours assessed by bromodeoxyuridine staining *in vitro* and *in vivo* and flow cytometry. *Cytometry, 6*, 641–647.

Withers, H R. & Peters, L J, 1980. Radiobiology of high-LET irradiation: neutron irradiation. In *Progress in Radio-Oncology*. Ed. by K.-H. Karcher, H. D Kogelnik and H.-J. Meyer (Georg Thieme Verlag, Stuttgart), pp. 1–7.

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Radiation response of multicellular spheroids initiated from five human melanoma xenograft lines. Relationship to the radioresponsiveness *in vivo*

By Einar K. Rofstad, Ph.D., Anne Wahl, M.Sc. and Tor Brustad, Ph.D.

Institute for Cancer Research and The Norwegian Cancer Society, The Norwegian Radium Hospital, Montebello, 0310 Oslo 3, Norway

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ABSTRACT

Multicellular spheroids, initiated from five human melanoma xenograft lines (E.E., E.F., G.E., M.F., V.N.) and grown in liquid-overlay culture, were characterised with regard to radiation response. The principal aim of the work was to search for possible correlations with the radioresponsiveness *in vivo* of the parent xenografts. The spheroids were 100 ± 5 μm in diameter at irradiation and did not contain radiobiologically hypoxic cells. Single-cell survival measured in soft agar, specific growth delay and spheroid cure were used as end-points The cellular radiosensitivity was the same whether a melanoma was grown as spheroids or as xenografts. An intercellular contact effect was found for spheroids of the G.E. melanoma but not for spheroids of the E.E., E.F., M.F. and V.N. melanomas, in agreement with previous observations from studies of the corresponding xenografts *in vivo* A positive correlation was found between the radiation response of the spheroids, measured as cell survival after 6 Gy or as specific growth delay after 6 Gy, and the radiation response of the parent tumours, measured as specific growth delay after 15 Gy. There was no correlation between the SCD_{50} (the dose required to cure 50% of the spheroids) and the radioresponsiveness *in vivo*. It is concluded that differences in radioresponsiveness *in vivo* among tumours may be identified from studies of the corresponding multicellular spheroids grown in liquid-overlay culture

Clinical investigations have indicated that the radiocurability of human tumours differs considerably among individual patients and may depend on histological type and differentiation status (Rubin et al, 1974). However, histology is probably not a major determinant of radiocurability since different tumours with similar histological appearance may require totally different doses to be locally controlled (Thames et al, 1980; Peters & Fletcher, 1983). Thus, there is a need for predictive assays for assessment of the clinical radiocurability of tumours.

Multicellular spheroids are an *in-vitro* tumour model with several biological characteristics in common with solid tumours (Sutherland & Durand, 1976). Large spheroids have diffusion gradients for oxygen, glucose and other nutrients, resulting in necrotic areas, radiobiologically hypoxic cells and cells at reduced pH (Sutherland & Durand, 1973; Acker, 1984). Important radiobiological phenomena such as contact effect (Durand & Sutherland, 1972), repair processes (Sutherland & Durand, 1973; Durand & Sutherland, 1976) and reoxygenation (Durand & Sutherland, 1976) have been demonstrated for several spheroid systems. Moreover, spheroids initiated from different cell lines show individual and characteristic growth parameters, *e.g.* volume-doubling time, cell cycle distribution, cell density and intercellular adhesiveness (Carlsson et al, 1983; Rofstad et al, 1986).

The present work was aimed at investigating the potential of multicellular spheroids in predicting the radiocurability of tumours *in vivo*. Spheroids were initiated from disaggregated human melanoma xenografts and grown in liquid-overlay culture (Yuhas et al, 1977). Radiation response was measured as cell survival in soft agar, growth delay and spheroid cure, and discussed in relation to the radioresponsiveness *in vivo* of the parent melanoma xenografts (Rofstad & Brustad, 1985).

MATERIALS AND METHODS

Xenografts

Five human melanoma xenograft lines (E.E., E.F., G.E., M.F., V.N.), originally derived from lymph-node metastases of patients admitted to The Norwegian Radium Hospital, were used in the present work. Tumour tissue was transplanted directly into athymic mice (BALB/c/nu/nu/BOM) without previous adaptation to *in-vitro* culture conditions. Histologically, the metastases were composed of melanin-poor atypical naevus cells growing in large spheres Cells and nuclei varied greatly in size and shape, and numerous mitotic figures were seen.

The melanomas were grown serially in athymic mice by implanting fragments, approximately 2 mm × 2 mm × 2 mm in size, subcutaneously into the flanks of recipient mice. Passages 35–60 of the xenografts in athymic mice were used to grow the spheroids studied in the present work. Light and electron microscopic examinations showed that the histological appearance of the xenografts in these passages was similar to that of the metastases from which they were derived. The radiation response of the xenografts, measured as specific growth delay, has been previously reported (Rofstad & Brustad, 1985).

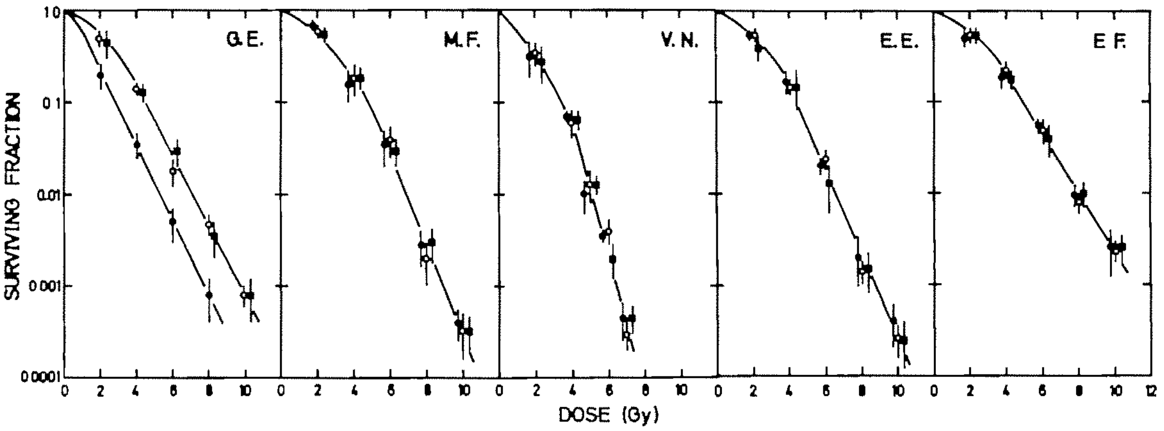

FIG 1.

X-ray survival curves for human melanoma spheroids grown in liquid-overlay culture The spheroids were disaggregated immediately before irradiation (●), immediately after irradiation (○) or 18 h after irradiation (■). Each point represents the mean surviving fraction from three to six independent experiments. The vertical bars represent standard errors. The surviving fractions from each individual experiment were calculated from the mean number of colonies in four tubes with irradiated cells and four tubes with unirradiated cells

Spheroids

Single-cell suspensions prepared by mechanical disaggregation of the mouse-flank tumours were used to grow spheroids. The culture medium was Ham's F12 supplemented with 20% fetal calf serum, 250 mg/l penicillin and 50 mg/l streptomycin (Gibco-Biocult, Glasgow). Care was taken to ensure that the experimental procedure and the growth conditions were equal for all spheroid cultures. Approximately 1.5×10^6 cells in 30 ml medium were seeded in 75 cm^2 plastic tissue culture flasks (Falcon, Oxnard) coated with a thin layer (3 ml per flask) of 1% agar (Bacto agar, Difco, Detroit). The flasks were then agitated (10 periods per min) at 37°C for 2 h using a tilting platform (Rotary Mixer, Cenco. Inst., Breda) and aggregates, approximately 50 μm in diameter, were formed. One day later, about 500 aggregates were transferred to 75 cm^2 coated culture flasks and cultivated in 30 ml medium (liquid-overlay culture). The agar coating prevented attachment of spheroids to the bottom of the flasks. The culture medium was changed three times a week. The volume-doubling times of the spheroids under these conditions were 1.8±0.2 days (E.E., E.F.), 2.0±0.3 days (G.E.), 1.7±0.2 days (M.F.) and 2.7±0.4 days (V.N.) up to a diameter of about 300 μm (Rofstad et al, 1986). The spheroids had a diameter of 100±5 μm when they were irradiated. The number of cells per spheroid was measured to be in the range 400–500. Spheroids of this size had not developed central necrosis. Histologically and cytologically, the spheroids were similar to the parent xenografts (Rofstad et al, 1986).

Irradiation

An X-ray unit (Siemens Stabilipan, Erlangen), operated at 220 kV, 19–20 mA, and with 0.5 mm Cu filtration, was used for irradiation. Spheroid suspensions as well as suspensions of cells prepared from spheroids were irradiated under aerobic conditions at a dose-rate of 3.0 Gy per min. The suspensions were kept in Carrel flasks during exposure. The irradiation was performed at room temperature

Radiation response assays

Survival of single cells was measured by using the soft-agar colony assay developed by Courtenay and Mills (1978). Single cells were obtained by treating the spheroids with a 0.05% trypsin/0.02% EDTA solution for 10 min at 37°C. The spheroids were disaggregated completely by this treatment and almost 100% of the cells appeared to be morphologically intact. Cell concentrations were determined with a haemocytometer viewed through a phase-contrast microscope. The soft agar was prepared from powdered agar (Bacto agar, Difco, Detroit) and Ham's F12 culture medium with 20% fetal calf serum, 250 mg/l penicillin and 50 mg/l streptomycin (Gibco-Biocult, Glasgow). Erythrocytes from August rats and melanoma cells were added as previously described (Rofstad, 1981). Aliquots of 1 ml of soft agar with the appropriate number of melanoma cells were seeded in plastic tubes (Falcon 2057, Oxnard). The cells were incubated at 37°C for 3–4 weeks (E.E., E.F.), 4–5 weeks (M.F., V.N.) or 5–6 weeks (G.E.) in an atmosphere of 5% O_2, 5% CO_2 and 90% N_2. Culture medium (2 ml) was added on the top of the agar 5 days after seeding and then changed weekly. Colonies were counted with a stereomicroscope. Cells giving rise to colonies larger than 50 cells were scored as surviving. The plating efficiency of untreated cells was 15–40% (E.E., M.F., V.N.), 50–80% (E.F.) and 5–15% (G.E.) and independent of the number of cells seeded (in the range 100–5000 cells per tube). Heavily irradiated "feeder" cells (100 Gy), up to 100 000 cells per tube, neither enhanced the plating efficiency nor changed the surviving fraction of irradiated cells. Consequently, such "feeder" cells were not used in the present work. Details of the experimental procedure are reported elsewhere (Rofstad, 1981).

Growth delay after irradiation was determined by cultivating irradiated and unirradiated spheroids in liquid-overlay culture. Spheroid diameters were measured with an ocular micrometer in an inverted phase-contrast microscope. The time taken for the irradiated (T_5') and the unirradiated (T_5) spheroids to reach five times their volume at treatment was recorded. Specific growth delay was calculated as $(T_5'-T_5)/T_2$, where T_2 is the mean volume-doubling time of the unirradiated spheroids (Hermens & Barendsen, 1975; Steel et al, 1983).

Spheroid cure was measured by plating spheroids in uncoated wells of 96-well culture plates (Nunclon, A/S Nunc, Roskilde). The spheroids attached to the bottom of the wells with subsequent cellular outgrowth. According to the criteria developed by Carlsson and Nederman (1983), a spheroid was scored as surviving if the outgrowth resulted in more than 1000 cells within 5 weeks. Generally, the surviving spheroids could be easily distinguished from the cured ones since the outgrowth in the latter case usually resulted in less than 100 cells before the layer of outgrowing cells disintegrated 2 weeks after irradiation. Unirradiated spheroids always fulfilled the criteria for a spheroid to be scored as surviving.

Results

Figure 1 shows survival curves for the melanoma cells after exposure to X rays. The melanomas were grown as spheroids and irradiated as single cells, or grown and irradiated as spheroids and assayed as single cells immediately after or 18 h after irradiation. The cell yield from spheroids disaggregated immediately after and 18 h after irradiation was not significantly different, suggesting that cell lysis did not occur during this time interval. The G.E. melanoma showed a significant contact effect, whereas the other four melanomas did not. There was no evidence of potentially lethal damage (PLD) repair or presence of radiobiologically hypoxic cells in the spheroids.

Mean relative spheroid volume for the E.E., G.E. and M.F. melanomas as a function of time after irradiation with doses up to 7 Gy is shown in Fig. 2. The data in Fig. 2 refer to one single experiment with each of the melanomas. Four to five such experiments were carried out and formed the basis for calculation of specific growth delay. Figure 3 shows that specific growth delay increased with increasing radiation dose. The E.F. and V.N. melanomas formed loosely packed spheroids with an irregular shape (Rofstad et al, 1986). Reproducible growth delay data could not be established for these melanomas because single cells and fragments broke away from the spheroids after irradiation.

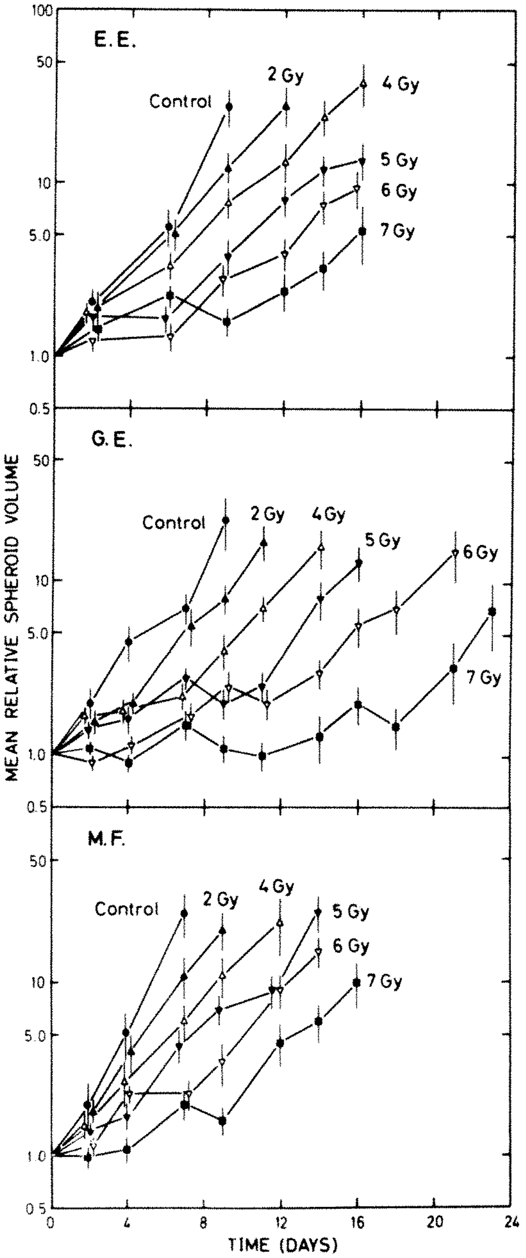

Fig. 2.

Mean relative volume for human melanoma spheroids grown in liquid-overlay culture as a function of time after irradiation. Each curve is based on 30–50 spheroids. The vertical bars represent standard errors.

Figure 4 shows percentage of spheroid cure as a function of radiation dose for the E.E., G.E., M.F. and V.N. melanomas. Four to seven experiments were carried out with each of the melanomas, and the results in Fig. 4 refer to single experiments. Dose–response

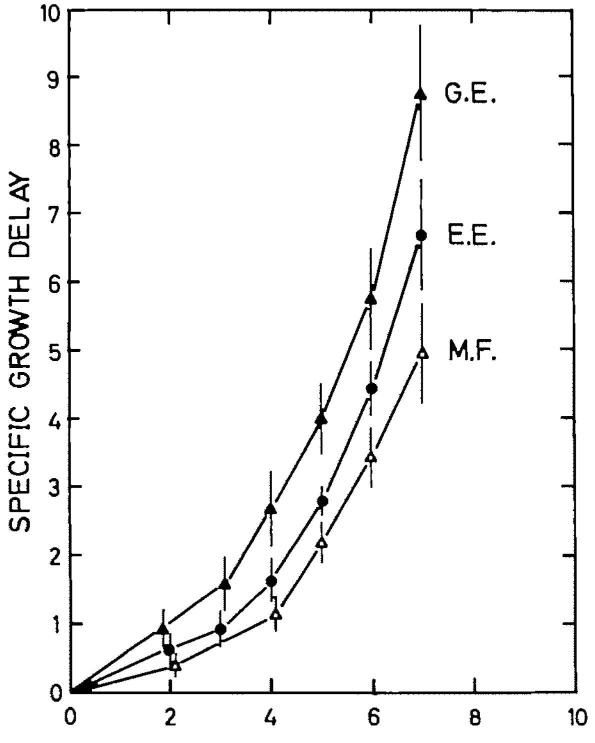

Fig. 3.

Specific growth delay for human melanoma spheroids grown in liquid-overlay culture as a function of radiation dose. Each point is based on four or five independent experiments, each involving 30–50 spheroids. The vertical bars represent standard errors.

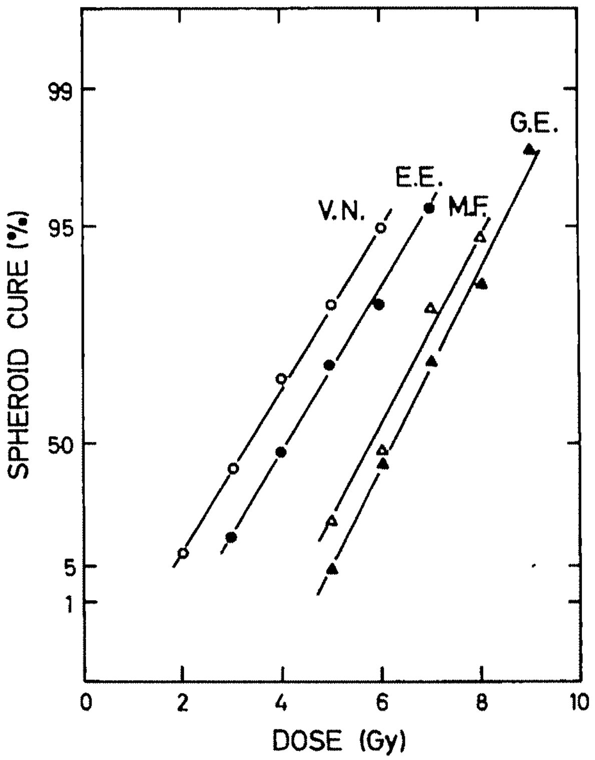

Fig. 4.

Percentage cure for human melanoma spheroids assayed in microwells as a function of radiation dose. The data are plotted on a double negative logarithmic ordinate. Each point is based on 60 spheroids.

curves based on the method of double negative logs (Gilbert, 1979; Moore & Hendry, 1984) were fitted to the data by regression analysis. The SCD_{50} was calculated from each data set using the relationships:

$$-\ln(-\ln P) = \frac{1}{D_0}D - \ln(Nn) \qquad (1)$$

$$SCD_{50} = D_0[\ln(Nn) - \ln(\ln 2)] \qquad (2)$$

where P is the probability of spheroid cure, n the extrapolation number of the cell survival curve and N the number of stem cells per spheroid. The SCD_{50} was found to be 4.4±0.3 Gy (E.E.), 6.6±0.3 Gy (G.E.), 5.8±0.5 Gy (M.F.) and 3.6±0.2 Gy (V.N.). Measurement of spheroid cure by the present procedure did not give reproducible results for the E.F. melanoma.

The rankings of the melanomas in radiosensitivity were V.N. > G.E. > E.E. > M.F. > E.F. when cell survival (6 Gy; disaggregation immediately after irradiation) was used as end-point (Fig. 1), G.E. > E.E. > M.F. when specific growth delay was used as end-point (Fig. 3), and V.N. > E.E. > M.F. > G.E. when SCD_{50} was used as end-point (Fig. 4). Thus, there was agreement between the specific growth delay and the cell survival rankings (Fig. 5A). However, there was no correlation between SCD_{50} and cell survival (Fig. 5B).

Discussion

The oxygen concentration at the surface of spheroids growing in liquid-overlay culture cannot be kept constant during an experiment due to increased oxygen consumption with increasing spheroid size, changes of culture medium and agitation of the medium during handling of the culture flasks (Franko et al, 1984). Nevertheless, our melanoma spheroids showed constant volume-doubling times up to a diameter of about 300 μm (Rofstad et al, 1986), and the radiation responses were highly reproducible. The spheroids had a diameter of 100±5 μm when they were irradiated. Histological examinations have revealed that spheroids of this size have not developed central necrosis (Rofstad et al, 1986). Evidence that the spheroids contained radiobiologically hypoxic cells was not found, even though the irradiation was carried out at room temperature and not at 37°C (Fig. 1). Moreover, the survival curves for cells irradiated after disaggregation

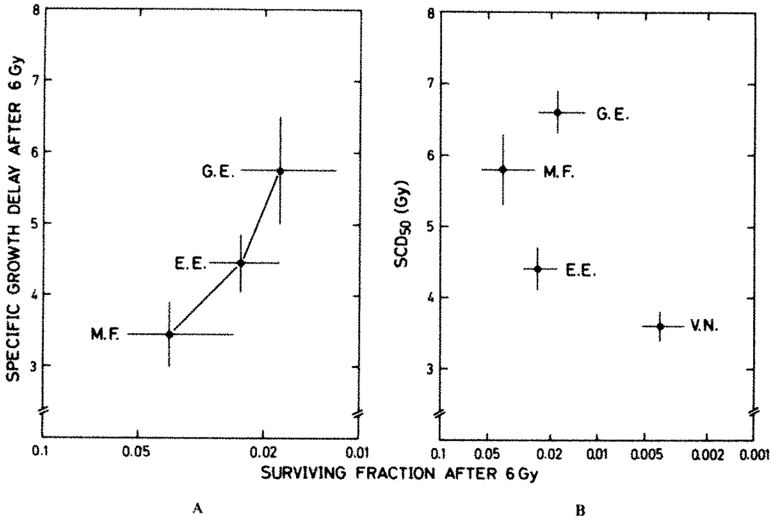

Fig. 5.

Specific growth delay after 6 Gy (A) and SCD$_{50}$ (B) versus surviving fraction after 6 Gy measured in soft agar for human melanoma spheroids. The surviving fractions after 6 Gy refer to spheroids disaggregated immediately after irradiation. The bars represent standard errors.

of the spheroids were equal to those previously reported for cells from disaggregated tumours of the same melanomas (Rofstad & Brustad, 1981), *i.e.* the cellular radiosensitivity was the same whether the cells were grown as spheroids in liquid-overlay culture or as solid tumours *in vivo*. Consequently, the spheroid cultures studied in the present work were stable *in-vitro* models of the aerobic compartments of the parent tumour xenografts.

The survival curves for spheroids disaggregated immediately after and 18 h after irradiation were not significantly different for any of the melanomas (Fig. 1), *i.e.* there was no evidence of PLD repair. Potentially lethal damage repair has been demonstrated to occur in

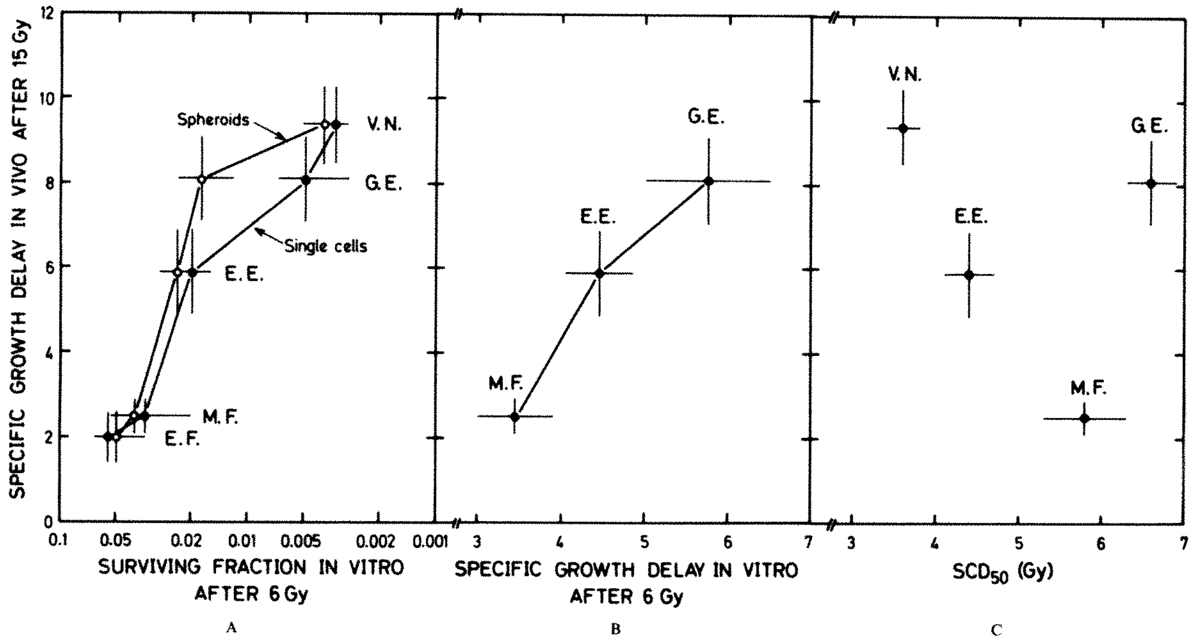

Fig. 6.

Radiation response *in vivo* (xenografts) versus radiation response *in vitro* (spheroids) for human melanomas. Specific growth delay after 15 Gy is used as a measure of response *in vivo*. Surviving fraction after 6 Gy measured in soft agar (A), specific growth delay after 6 Gy (B) and SCD$_{50}$ (C) are used as a measure of response *in vitro*. The surviving fractions after 6 Gy refer to spheroids disaggregated immediately before (single cells) or immediately after (spheroids) irradiation. The bars represent standard errors.

the parent xenografts *in vivo* (Rofstad, 1981). This apparent discrepancy was probably a consequence of differences in oxygenation and cell proliferation due to differences in size, and does not represent a fundamental difference between the spheroids and the tumours. The PLD repair *in vivo* took place mainly in hypoxic, non-proliferating cells (Rofstad, 1981) and this compartment of the tumours was not modelled by the spheroids studied here.

An intercellular contact effect similar to that reported for V79 Chinese hamster spheroids (Durand & Sutherland, 1972) was found for the G.E. melanoma, but not for the E.E., E.F., M.F. and V.N. melanomas (Fig. 1). We have previously reported that a contact effect is not present in the E.E. and V.N. melanomas *in vivo* (Rofstad & Brustad, 1983). Similar, unpublished studies have demonstrated to contact effect in the G.E. melanoma *in vivo*, whereas no evidence of a contact effect was found for the E.F. and M.F. melanomas *in vivo*. Thus, there was complete agreement between the spheroid and xenograft studies. Our observations are in agreement with conclusions drawn in an extensive review by Rasey (1983); some tumours and spheroid cultures show a pronounced contact effect whereas others do not, *i.e.* a contact effect is not a general phenomenon. Recently, Dertinger et al (1984) presented evidence that a contact effect is present only in cells that are electrically coupled via gap junctions.

One objective of the present study was to investigate whether it would be possible to identify differences in the radioresponsiveness *in vivo* among the parent xenografts from the radiation response of the spheroids. The five spheroid types showed individual and characteristic responses to radiation, irrespective of the end-point considered (Figs 1, 3 and 4). The radiation response *in vivo* of the parent xenografts has been previously studied by using growth delay as the end-point (Rofstad & Brustad, 1985). A procedure for determining the relative radioresponsiveness of tumours on the basis of growth delay data has not been agreed upon (Trott, 1983). However, specific growth delay after 15 Gy has been found to be a suitable parameter for the radioresponsiveness of our melanoma xenografts (Rofstad & Brustad, 1985). Figure 6 shows specific growth delay *in vivo* after 15 Gy plotted against the radiation response of the corresponding spheroids. Surviving fraction after 6 Gy measured in soft agar, specific growth delay after 6 Gy, and SCD_{50} were used as parameters for the radiation response of the spheroids. Spheroids irradiated with 6 Gy showed cell survival levels in the same range as tumours exposed to 15 Gy *in vivo* (Flaten et al, 1981; Rofstad, 1981).

A clear correlation was found between specific growth delay *in vivo* after 15 Gy and surviving fraction *in vitro* after 6 Gy, irrespective of whether the spheroids were disaggregated immediately before or immediately after irradiation (Fig. 6A). This observation suggests that it may be possible to develop assays for prediction of the radioresponsiveness *in vivo* of tumours based on the radiosensitivity of the corresponding spheroids, measured as cell survival in soft agar.

Specific growth delay *in vivo* after 15 Gy increased with increasing specific growth delay *in vitro* after 6 Gy (Fig. 6B). The latter parameter may have been influenced by several factors in addition to the fraction of surviving cells. Firstly, radiation effects on the rate of cell proliferation may have affected the growth delay. Secondly, radiation-inactivated cells may not have been broken down and removed completely at the time a mean relative volume of 5.0 was reached, *i.e.* radiation-inactivated cells may have contributed to the volume of the irradiated spheroids and hence to an artificially short growth delay. Thirdly, a considerable fraction of the spheroids was cured after 6 Gy, *i.e.* the measured growth delays refer to uncured spheroids only. Nevertheless, Fig. 6B suggests that spheroid growth delay data may be utilised to identify differences in radioresponsiveness *in vivo* among tumours. Observations by Deacon et al (1985) also support this possibility; they studied a human neuroblastoma and found nearly equal specific growth delays after irradiation of xenografted tumours and spheroids.

No correlation was found between specific growth delay *in vivo* after 15 Gy and SCD_{50} (Fig. 6C). The SCD_{50} was not correlated to the cell survival measured for the spheroids after exposure to 6 Gy either (Fig. 5B). These observations may reflect that a significant fraction of the surviving stem cells in the spheroids died of other causes than radiation damage before they were able to migrate out of the spheroids, attach to the plastic surface and initiate outgrowth. In fact, it can be shown by use of Equation 2 that the number of effective stem cells per spheroid in the spheroid cure experiments was very low compared with the number of clonogenic cells per spheroid.

In conclusion, the present work suggests that multicellular spheroids have a significant potential in identifying differences in radioresponsiveness *in vivo* among tumours. Cell clonogenicity in soft agar seems to be a more suitable end-point than growth delay since it can be used for loosely as well as densely packed spheroids. Some tumours, such as the G.E. melanoma, show a significant contact effect whereas others do not, implying that spheroids may predict the radioresponsiveness of tumours more accurately than single cells. In fact, since there is some evidence that the clinical radioresponsiveness of tumours may be related to the initial slope of the cell survival curve (Fertil & Malaise, 1981; Deacon et al, 1984; Fertil & Malaise, 1985), it may be a prerequisite that an *in-vitro* predictive assay of radioresponsiveness records a possible contact effect. Our data are encouraging and further studies involving fractionated irradiation seem warranted.

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REFERENCES

Acker, H., 1984. Microenvironmental conditions in multicellular spheroids grown under liquid-overlay tissue culture conditions. In *Spheroids in Cancer Research Methods and Perspectives*. Ed. by H. Acker, J. Carlsson, R. Durand & R. M. Sutherland (Springer-Verlag, Berlin, Heidelberg), pp. 116–133.

Carlsson, J. & Nederman, T., 1983. A method to measure the radio- and chemosensitivity of human spheroids. *Advances in Experimental Medicine and Biology, 159*, 399–417.

Carlsson, J., Nilsson, K., Westermark, B., Pontén, J., Sundström, C., Larsson, E., Bergh, J., Påhlman, S., Busch, C & Collins, V. P., 1983. Formation and growth of multicellular spheroids of human origin. *International Journal of Cancer, 31*, 523–533.

Courtenay, V. D. & Mills, J., 1978. An *in vitro* colony assay for human tumours grown in immune-suppressed mice and treated *in vivo* with cytotoxic agents. *British Journal of Cancer, 37*, 261–268.

Deacon, J., Peckham, M. J & Steel, G. G., 1984. The radioresponsiveness of human tumours and the initial slope of the cell survival curve. *Radiotherapy and Oncology, 2*, 317–323.

Deacon, J. M., Wilson, P A. & Peckham, M. J, 1985. The radiobiology of human neuroblastoma. *Radiotherapy and Oncology, 3*, 201–209.

Dertinger, H., Guichard, M. & Malaise, E. P., 1984. Relationship between intercellular communication and radiosensitivity of human tumor xenografts. *European Journal of Cancer and Clinical Oncology, 20*, 561–566.

Durand, R E. & Sutherland, R M, 1972. Effects of intercellular contact on repair of radiation damage. *Experimental Cell Research, 71*, 75–80

——1976 Repair and reoxygenation following irradiation of an *in vitro* tumor model. *International Journal of Radiation Oncology, Biology, Physics, 1*, 1119–1124

Fertil, B. & Malaise, E P., 1981. Inherent cellular radiosensitivity as a basic concept for human tumor radiotherapy. *International Journal of Radiation Oncology, Biology, Physics, 7*, 621–629.

——1985 Intrinsic radiosensitivity of human cell lines is correlated with radioresponsiveness of human tumors: analysis of 101 published survival curves. *International Journal of Radiation Oncology, Biology, Physics, 11*, 1699–1707.

Flaten, T. P., Rofstad, E K. & Brustad, T., 1981. Radiation response of two human malignant melanomas grown in athymic nude mice. *European Journal of Cancer, 17*, 527–532.

Franko, A. J, Freedman, H I. & Koch, C J, 1984. Oxygen supply to spheroids in spinner and liquid-overlay culture. In *Spheroids in Cancer Research. Methods and Perspectives*. Ed by H. Acker, J. Carlsson, R Durand & R M. Sutherland (Springer-Verlag, Berlin, Heidelberg), pp. 162–167.

Gilbert, C. W., 1979. A double minus log transformation of mortality probabilities. *International Journal of Radiation Biology, 25*, 633–634

Hermens, A. F & Barendsen, G W., 1975 The importance of proliferation kinetics and clonogenicity of tumor cells for volume responses of experimental tumors after irradiation. In *Radiation Research, Biomedical, Chemical and Physical Perspectives*. Ed. by O. F Nygaard, H. I. Adler & W K Sinclair (Academic Press, New York), pp. 834–849.

Moore, J V. & Hendry, J. H., 1984. Relationship of clonogenic cells and "tumour-rescuing cells", modelled in irradiated spheroids *in vitro*. *British Journal of Radiology, 57*, 935–937.

Peters, L. J & Fletcher, G H., 1983 Causes of failure of radiotherapy in head and neck cancer *Radiotherapy and Oncology, 1*, 53–63.

Rasey, J. S, 1983. Cell-cell contact and repair of radiation damage. In *Radiation Research. Reviews and Summaries on Chemistry, Physics, Biology and Medicine. Proceedings of the Seventh International Congress of Radiation Research*. Ed. by J. J. Broerse, G. W. Barendsen, H. B Kal & A J van der Kogel (Martinus Nijhoff Publishers, Amsterdam), pp 303–310.

Rofstad, E K., 1981 Radiation response of the cells of a human malignant melanoma xenograft. Effect of hypoxic cell radiosensitizers. *Radiation Research, 87*, 670–683.

Rofstad, E. K. & Brustad, T., 1981. Radiation response *in vitro* of cells from five human malignant melanoma xenografts. *International Journal of Radiation Biology, 40*, 677–680.

——1983 Intercellular contact and the radiation response of cells of human melanoma xenografts *International Journal of Radiation Oncology, Biology, Physics, 9*, 191–195.

——1985 Tumour growth delay following single dose irradiation of human melanoma xenografts. Correlations with tumour growth parameters, vascular structure and cellular radiosensitivity. *British Journal of Cancer, 51*, 201–210

Rofstad, E. K., Wahl, A, Davies, C. de L & Brustad, T, 1986. Growth characteristics of human melanoma multicellular spheroids in liquid-overlay culture: comparisons with the parent tumour xenografts. *Cell and Tissue Kinetics, 19*, 205–216

Rubin, P., Keller, B. & Quick, R., 1974. The range of prescribed tumor lethal doses (PTLD) in the treatment of different human tumors. In *The Biological and Clinical Basis of Radiosensitivity*. Ed. by M. Friedman (Charles C Thomas, Springfield), pp. 435–484.

Steel, G G, Courtenay, V. D. & Peckham, M J, 1983 The response to chemotherapy of a variety of human tumour xenografts. *British Journal of Cancer, 47*, 1–13.

Sutherland, R. M. & Durand, R. E., 1973 Hypoxic cells in an *in vitro* tumour model. *International Journal of Radiation Biology, 23*, 235–246.

——1976. Radiation response of multicell spheroids—an *in vitro* tumour model. *Current Topics in Radiation Research Quarterly, 11*, 87–139.

Thames, H. D., Peters, L. J., Spanos, W. & Fletcher, G. H., 1980. Dose response of squamous cell carcinomas of the upper respiratory and digestive tracts. *British Journal of Cancer, 41, (Suppl 4)*, 35–38

Trott, K. R., 1983. Human tumour radiobiology: clinical data. *Strahlentherapie, 159*, 393–397

Yuhas, J. M., Li, A. P, Martinez, A. O. & Ladman, A. J., 1977 A simplified method for production and growth of multicellular tumor spheroids. *Cancer Research, 37*, 3639–3643.

Book reviews

Atlas of Normal Fetal Ultrasonographic Anatomy. By R. A. Bowerman, pp. viii + 154 + index, 1986 (Blackwell Scientific, Oxford/Year Book Medical, Chicago), £38.00.
ISBN 0–8151–1104–5

While this book is primarily an atlas, there are two introductory chapters about fetal scanning and fetal well-being. These are concise, covering only six pages in all, but as a brief review of the techniques and indications for scanning they are adequate. It could be argued that in an atlas this is unnecessary, but as a means of setting the scene for those with little experience of scanning they may be useful. The remainder of the book is, without any doubt, excellent. The images are of top quality. The fetus is dealt with systematically with multiple views of many parts, especially in the head. For the ultrasonographer who has been faced with an unusual projection and is not quite sure what he is seeing anatomically, this atlas solves most problems of what is normal.

Inevitably, there must be a few small quibbles: Fig. 4:15 shows measurement of head circumference on an image where part of the head is not shown and the position to place the calipers has to be guessed. No mention is made of the inaccuracy such a technique suffers from. Page 58 mentions assigning gestational age in the third trimester without pointing out the inaccuracies of this, even with the best images and most meticulous technique. On page 112 it is stated "..... normal prominent renal pelvis can be delineated from pathologically dilated pelvis by scanning over time." This is not so as the pelvis dilated due to vesico-ureteric reflux can behave in a similar manner, and to call all such patients normal may be somewhat ill-advised without further investigation after delivery.

In spite of these slight inaccuracies, this book fills a gap and can be thoroughly recommended to any department undertaking obstetric ultrasound scanning. It will be much used, particularly by those preparing for the D.M.U. exam.

D. W. PILLING

Computed Tomography. Assessment Criteria, CT System Technology, Clinical Applications. By J. Alexander, W. Kalender and G. Linke, pp 175, 1986 (Siemens Aktiengesellschaft, Berlin and Munich; Wiley, Chichester), £25.00.
ISBN 0–471–99842–7

The contents of this book lie in the grey area between disinterested scientific assessment and industrial sales promotion. Most of the technical and scientific development of X-ray computed tomography (CT) has occurred not in academic centres, but within industry. Thus technical literature from industrial authors is particularly valuable to users of CT systems to give a sound scientific understanding of their operation. This book provides a clear exposition of the Siemens view of the design, evaluation, use and cost-effectiveness of CT systems. Not surprisingly, it is concluded that rotate-rotate geometry and a pulsed generator are preferable. The advantages of solid-state detectors are promoted, while the benefits of high-pressure xenon detectors are not well discussed. However, before dismissing the volume as pure sales promotion, it must be said that there is great clarity in the discussion of the evaluation criteria for CT systems, containing much which could well be of value to any CT user. Contrast detail, noise structure, modulation transfer function measurement and its dependence upon geometry and reconstruction algorithm are all well considered. The illustrations are clear and, in particular, the CT image reproduction is excellent. The chapter on clinical applications will have a larger readership among those who use a Siemens scanner, since the detail given for techniques of dynamic scanning, radiation treatment planning or dual-energy scanning is specific.

This book is a thoroughly practical text aimed primarily at users of Siemens CT equipment. It may also find some readership among those with a more general interest in the assessment and use of CT systems.

F. A. DUCK

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Technical notes

Simulation of patient loading in nuclear magnetic resonance imaging through the use of inductive damping loops

By S. J. Jennings, B.Sc., R. A. Lerski, B.Sc., Ph.D., D. W. McRobbie, M.Sc.,
K. Straughan, B.Sc., A.R.C.S. and J. S. Orr, D.Sc.

Department of Medical Physics, Royal Postgraduate Medical School, Hammersmith Hospital, London

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The quantitative assessment of the imaging performance of nuclear magnetic resonance (NMR) scanning equipment requires the use of test objects (Orr et al, 1983; Lerski et al, 1984). These are commonly constructed from perspex and are filled with aqueous solutions of paramagnetic salts (*e.g.* $CuSO_4$ or $MnCl_2$) to provide the NMR signal with a relaxation behaviour (T_1 in particular) similar to tissue. The presence of the human body during the NMR imaging procedure has the effect of loading the receiver coil. This is due to energy dissipation by currents induced in the conducting tissue. The solutions of paramagnetic salts do not provide conducting pathways and subsequently have very little loading effect. The signal-to-noise ratio is degraded by coil loading and falsely high values will be obtained if measurements are made without matching this effect when using test objects. Saline-filled containers can be used to load receiver coils, but these may be difficult to construct and may interfere with the positioning of the test objects. The use of an inductive damping loop has been proposed as an alternative method of matching coil loading (Edelstein et al, 1984). This consists of an inductive loop together with a tuning capacitor and a resistance, all in series (Fig. 1).

The investigation reported here considers the use of such loops with head coils, the appropriate values of inductance and the values of resistance required. The possible use of a standard loop to provide appropriate damping for a number of different head coils, at a range of pre-amplifier loadings and for different frequencies, is also considered. The normal variation of head loading by different subjects and the day-to-day variation for one subject are reported.

TECHNIQUE

The four receiver coils investigated were used with a research resistive 0.1 T NMR scanner constructed in the Medical Physics Department, Hammersmith Hospital. Geometrical details of the coils, three saddle coils and one spherical coil (Bydder et al, 1985), are given in Table I.

The quality factors (Q) of the coils were used to quantify their loading, this being measured by injecting a signal into the coil and measuring the voltage across a pick-up coil using a Hewlett Packard 3585A spectrum analyser. This is similar to the method described by Hoult (1978), except that the signal was injected using a cable terminated with a resistor in the proximity of the NMR receiver coil. The pick-up coil was positioned on the axis of the receiver coil and 5 cm away from the plastic former. The terminating resistor was placed opposite, but off axis, and 3 cm outward from the nearest conductor. During measurement, except where otherwise stated, the coils were placed on a non-conducting support about 0.6 m above a conducting ground plane which forms the floor of the NMR scanning laboratory. The signal used to excite the coil was derived from the tracking generator output of the spectrum analyser and was of constant magnitude when swept over the range of interest. Q was evaluated as the ratio of the frequency of peak response to the 3 dB bandwidth, both quantities being measurable directly on the spectrum analyser using cursors.

The inductive damping loops were made of one, two or three turns of copper wire of diameter 20 cm, or two or three turns of diameter 17.5 cm. The inductances of the loops were measured using a Hewlett Packard 4815A vector impedance meter and were tuned by adding a capacitance in series so that the impedance was wholly real at 4.25 MHz. The vector impedance meter was then disconnected and a resistor added in series to close the circuit (Fig. 1). The value of this

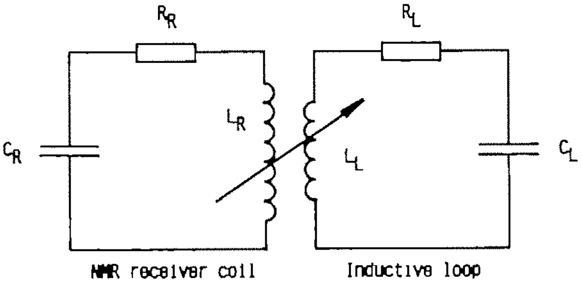

FIG 1.

Circuit diagram of an inductive damping loop shown alongside a receiver coil. L_R = receiver coil inductance, C_R = tuning capacitance, R_R = resistive component of L_R, L_L = inductance of damping loop, R_L = damping resistance (≫ resistive component of L_L), C_L = damping loop tuning capacitor

TABLE I

GEOMETRIC DETAILS OF THE RECEIVER COILS

Coil	Length (cm)	Diameter (cm)	No of turns	Inductance (μH)
Saddle 1	25	27	2×2	0.94
Saddle 2	25	27	2×2	1.14
Saddle 3	38	28	2×2	1.54
Spherical	—	23	2×4	1.61

resistance was determined by the experiments as described below.

Procedure and Results

Use of inductive damping loops to load NMR receiver coils

Saddle Coil 1 and the spherical coil were each tuned to 4.25 MHz using parallel capacitances. For both coils, Q was measured when unloaded, when loaded with a head and when loaded with a damping loop. In each case a range of resistances was used with the two-turn, 20 cm-diameter loop.

The Q of the saddle coil was brought down from an unloaded value of 295 to 217 when loaded with a head and that of the spherical coil from 406 to 184 (mean of four measurements from one subject). The frequency of peak response was lowered by < 2.5 kHz for the saddle coil and < 6.5 kHz for the spherical coil. Using the damping loops it was possible to lower Q to any desired value with appropriate series resistance. This also had the effect of lowering the frequency of peak response by about 2 kHz in the case of the saddle coil and about 3 kHz for the spherical coil.

Day-to-day and subject variation

The following experiments were performed in order to assess the natural variation of the effect of head loading on values of Q of the NMR receiver coil. In the first experiment variation between days for one subject using all of the coils was studied. In the second experiment the intersubject variation was determined with data from 27 subjects for one receiver coil. This will provide a standard against which the performance of the damping loops may be assessed.

The three saddle-type and the spherical receiver coils were each tuned to 4.25 MHz. The excitation and pick-up transducers, associated with the measurement of Q, were positioned within 0.5 cm on each occasion. On six different days Q was measured five times for each coil when unloaded and when loaded with a head. Table II shows the mean of all the measurements for each coil, the standard deviation between the daily means and the standard deviation between measurements, having removed the effect of the day-to-day variation. The measurements which show significant ($p < 0.05$) or highly significant ($p < 0.01$) variations between days, using one-way analysis of variance, are marked with one or two asterisks, respectively.

TABLE II

DAY-TO-DAY VARIATION OF Q FOR ONE SUBJECT

	Mean	SD (between days)	SD (between measurements)
Saddle Coil 1			
Unloaded	339	12.2	2.2**
Loaded	234	5.8	3.1**
Saddle Coil 2			
Unloaded	296	4.7	1.3**
Loaded	215	4.1	3.0**
Saddle Coil 3			
Unloaded	383	7.3	1.9**
Loaded	289	6.6	3.8**
Spherical			
Unloaded	382	3.7	2.9**
Loaded	194	4.9	6.4*

$^{*}p < 0.05$ (significant); $^{**}p < 0.01$ (highly significant).

The intersubject variation was investigated by comparing the Qs resulting from loading by 27 subjects (14 female, 13 male). In this experiment the receiver coil was placed in a room without a ground plane and at least 1 m away from any conductor, other than the experimental apparatus. Saddle Coil 2 was tuned to 4.25 MHz and Q was measured without loading and with each of the subjects. The unloaded Q of 274 (mean of 10 measurements) was lowered to 227±6 by female subjects, to 211±7 by male subjects and to 219±10 by male and female subjects grouped together (mean ± standard deviation of means of five measurements for each subject). The frequency of peak response was depressed by less than 1 kHz in all females and less than 2 kHz in all males.

Effect of damping-loop geometry

Saddle Coils 1 and 3 and the spherical coil were investigated to determine the values of resistance required to simulate the loading of a head. The Q of each coil was measured, when unloaded, loaded with a head and loaded with a one-, two- or three-turn 20 cm-diameter loop, or a two- or three-turn 17.5 cm-diameter loop. Their inductances were 0.81, 2.47, 5.24, 2.02 and 4.12 μH, respectively, and they were tuned with capacitors to 4.25 MHz. In each case the resistance of the loop was adjusted to match the effect of a head, and resistance values greater and smaller than the optimum value were tried to determine the sensitivity of Q to resistance changes.

Each of the three head coils had a different unloaded Q. The presence of a head reduced Q in each case by a different amount and tended to lower the frequency of peak response by 1 or 2 kHz. It was possible in all cases to simulate the effect of a head on Q with appropriate resistance values, but the lowering of the peak response frequency could not be matched at the same time. The resistances required with each of the two-turn loops

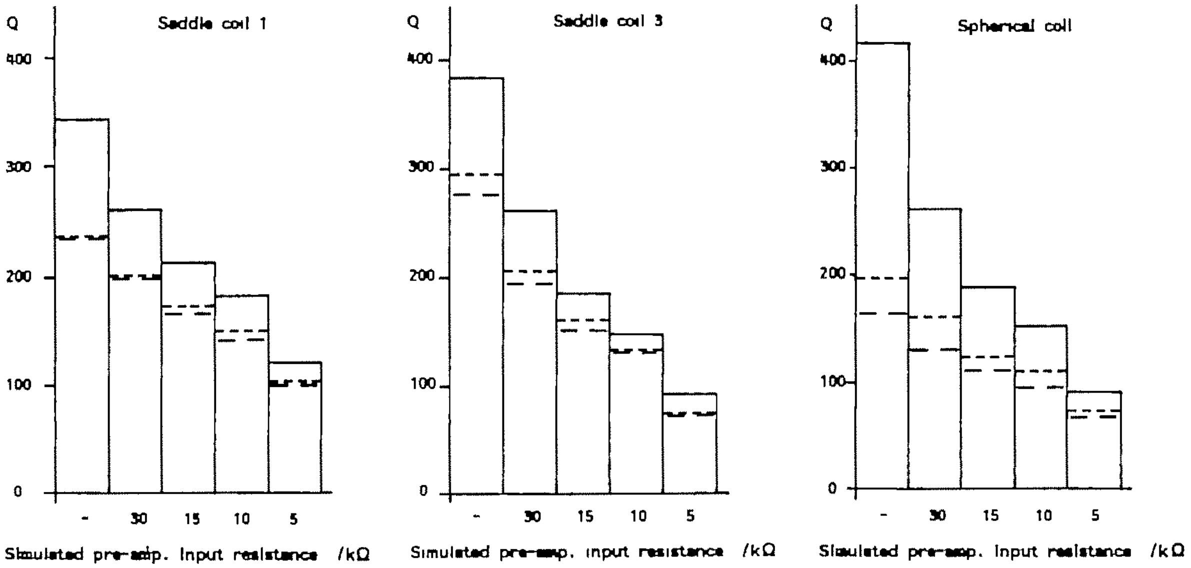

FIG. 2.

Effect of pre-amplifier loading on measured Q values for Saddle Coils 1 and 3 and the spherical coil, using a two-turn 17.5 cm-diameter damping loop compared with the effect of a head (—— unloaded, ---- loaded with head, — — loaded with inductive loop).

were within 0.5% of 2.07 kΩ for the 20 cm loop and within 3.5% of 0.96 kΩ for the 17.5 cm loop. Less consistent results were found for the other loops, where 12.5%, 12.6% and 29% were the figures for the one-turn 17.5 cm-diameter loop and three-turn 17.5 cm- and 20 cm-diameter loops, respectively.

The sensitivity of Q to loop resistance, evaluated as the ratio of fractional change in Q to fractional change in resistance, was less than unity for each coil and loop combination.

Variation with frequency

Saddle Coil 1 was tuned to 4.25 MHz and Q measured when unloaded, loaded with a head and loaded with a two-turn 20 cm-diameter loop. The resistance of the loop was adjusted to match the effects of the head and this was repeated with the coil and the loop retuned to 2.125 MHz and to 8.5 MHz. The loaded and unloaded Qs varied with frequency and, unfortunately, the resistance of the damping loop required to match head loading was neither constant nor linear over the range considered.

Effect of pre-amplifier loading

The Q of Saddle Coil 1 was measured when unloaded, loaded with a head, loaded with a two-turn 17.5 cm-diameter loop and loaded with a two-turn 20 cm-diameter loop. The resistances of the loops were then adjusted to match the effect of the head and kept constant for the rest of this part of the study. This sequence was repeated with a range of resistances (30 kΩ, 15 kΩ, 10 kΩ and 5 kΩ) across the connecting cable to model the effect of pre-amplifier loading. This was repeated using Saddle Coil 3 and the spherical coil but keeping the resistance of the damping loop unchanged at the value determined from the first coil.

The presence of a resistance across the pre-amplifier connection resulted, as expected, in a lowering of Q in each case, with and without further loading by a head or damping loop. With Saddle Coil 1, either of the damping loops resulted in a value of Q between 0% and −6% of that of the head at all values of pre-amplifier resistance. This compares with a discrepancy of between 15% and 45% when no damping loop was present. Using the same loop in the other saddle coil produced similar results, with a discrepancy of between 2% and 7% with damping compared with between 8% and 30% without. The match in loading was not so close for the spherical coil, with a discrepancy of between 10% and 18% with either of the damping loops compared with between 23% and 111% without any damping. The results, each representing the mean of two measurements, are presented in Fig. 2 (for clarity only the 17.5 cm-diameter loop is shown).

DISCUSSION AND CONCLUSIONS

Inductive damping can be used to lower the Q of a coil to any desired value and can be made to match the effect of a head in this respect. Some alteration of frequency occurs with head loading and in general this cannot be matched simultaneously with the correct Q, underlining the fact that inductive damping is not a complete model of the effect of a head.

A proportion of the loading caused by a head results from dielectric losses and no account of these are taken by this type of inductive damping loop. Steps may be taken to minimise this loss (Hoult & Lauterbur, 1979) but inductive losses are unavoidable. It should be noted that the same loops cannot be used for different frequencies, since readjustment of both resistance and tuning capacitance is required.

The quality factor of a coil is sensitive to surrounding conductors, including the investigator. It was found that standing close to an otherwise unloaded coil lowered Q by about 2%. Other factors such as the exact position and angle of the head and prevailing atmospheric conditions can also influence Q. This may account for the significant day-to-day variation and also the difference in unloaded values between the day-to-day and the intersubject variation experiments, which were performed in different rooms.

Although Coils 1 and 2 have the same dimensions and number of turns, their inductances are different. This may be because the conductors are of different thickness and different material is used for the insulators.

Our inductive damping loops were made by wrapping copper wire of cross-sectional area 1.5 mm^2 around circular formers. Using two turns around a diameter of 20 cm results in an inductance of around 2.5 μH which appears to be optimal for our receiver coils at a frequency of 4.25 MHz. In the above experiments the loops were tuned using a vector impedance meter. Alternatively, they may be tuned by soldering a trial capacitor in parallel and placing between an excitation source, such as a terminated cable and a pick-up coil, and adjusting the frequency to find the peak response. The correct capacitance to tune the loop can be calculated from the equation.

$$C_r = C_t[\omega_t/\omega_r]^2$$

where subscript t denotes trial and subscript r denotes required values. This may need to be repeated to achieve precise tuning. The resulting values are slightly different using this method but the effect on Q and frequency alteration of the receiver coil are comparable and the need for a vector impedance meter is avoided. When tuning has been achieved, a fixed or variable resistor is added such that all components are in series. Using any of the coils the resistance may be adjusted until the loading (as evaluated by Q) matches that of the head. The spectrum analyser greatly facilitates the measurement of Q but it can also be evaluated using a signal generator and oscilloscope by sweeping manually through frequency to find the 3 dB bandwidth.

It is possible to construct a fixed damping loop which can approximate the effect of a head in a number of different coils and when connected to a range of different pre-amplifier loadings. We have achieved this, at 4.25 MHz, for head coils through the use of a two-turn 20 cm-diameter loop loaded with 1.6 kΩ which Q-matched head loading to within 8% for the saddle coils and within 19% for the spherical coils These values should be compared with the coefficients of variation between days of 1.9% and between subjects of 4.7% for a saddle coil. The amplitude of the signal picked up by the receiver coil is proportional to Q and the signal-to-noise ratio to $\sqrt{Q}$ (Hoult & Richards, 1976). This suggests that the signal-to-noise ratio of the coils loaded with the damping loop would be within 5% of the head loading for the saddle coils, corresponding to a natural variation (based on one standard deviation) between subjects of 2.5% and within 10% for the spherical coil. However, for the best results the resistance of the loop should be readjusted for different coils or pre-amplifier loadings. The addition of the damping loop would, therefore, make the assessment of imaging systems more realistic when using test objects containing paramagnetic salts.

Acknowledgments

This work forms part of a combined project and acknowledgment is made to the Department of Health and Social Security, and in particular to Mr G. Higson and Mr J L. Williams for their support and encouragement.

REFERENCES

Bydder, G. M., Butson, P. C., Harman, R. R., Gilderdale, D. J. & Young, I. R., 1985. Use of spherical receiver coils in MR imaging of the brain. *Journal of Computer Assisted Tomography*, *9*, 413–414.

Edelstein, W. A., Bottomley, P. A. & Pfeifer, L. M., 1984. A signal to noise calibration procedure for NMR imaging systems. *Medical Physics*, *11*, 180–185.

Hoult, D I , 1978. The NMR receiver: a description and analysis of design *Progress in NMR Spectroscopy*, *12*, 41–77.

Hoult, D. I. & Lauterbur, P. C., 1979. The sensitivity of the zeugmatographic experiment involving human samples. *Journal of Magnetic Resonance*, *34*, 425–433.

Hoult, D. I. & Richards, R. E., 1976. The signal-to-noise ratio of the nuclear magnetic resonance experiment. *Journal of Magnetic Resonance*, *24*, 71–85

Lerski, R. A., Straughan, K & Orr, J. S., 1984. Calibration of proton density measurements in nuclear magnetic resonance imaging *Physics in Medicine and Biology*, *29*, 271–276

Orr, J S., Lerski, R A. & Straughan, K., 1983. Preliminary results from phantoms for spatial resolution, standardisation and calibration within NMR images. *Annali dell'Istituto Superiore di Sanita*, *19*, 191–196.

1986, *The British Journal of Radiology*, 59, 1035–1036

Technical notes

The use of simulator-based computed tomography in iridium-192 dosimetry

By C. J. Kotre, M.Sc., A.C.G.I., G. D. Lambert, M.Sc. and *P. J. D. K. Dawes, F.R.C.R.

Regional Medical Physics Department and *Regional Radiotherapy Centre, Newcastle General Hospital, Newcastle-upon-Tyne NE4 6BE

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When conventional radiography is used to determine the spatial distribution of brachytherapy sources, the interpretation of pairs of orthogonal radiographs may prove difficult, especially in the case of multiplane, or curved-plane implants. Where sources of uniform linear activity are implanted in a parallel array, as in the case of ^{192}Ir wire implants arranged in the Paris system, and running in a superior–inferior direction, cross-sectional information can provide a useful addition to, and in many cases a substitute for, conventional radiography. A computed tomography (CT) system based on a radiotherapy simulator (Kotre et al, 1984) has been employed to provide this information.

Patients are scanned immediately following the surgical implantation of the source guide tubes, 0.8 mm diameter lead solder wires having been placed in the tubes as markers. Since the ends of the marker wires are visible on the skin surface, it is a straightforward matter to position the scan section midway between the superior and inferior extent of the implant. Taking advantage of the large scan aperture available on the simulator, the patient can be positioned with the implant centred in the reconstruction area. A certain amount of couch twist may also be applied to provide a CT cut orthogonal to the axis of the source distribution. These positional requirements would be difficult to achieve on a conventional diagnostic CT scanner with a curved couch and limited scan aperture. The images produced are of a much lower quality than diagnostic CT images, but the positions of the marker wires are clearly defined, as are major anatomical landmarks. The simulator-based CT system has the additional advantages of low cost and unrestricted access for radiotherapy use.

Figures 1 and 2 show a simulator CT scan of a single-plane breast implant. Figure 2 is a digitally zoomed view of just the region around the implant. The six wires of the implant and most of the surrounding gross anatomy can be distinguished. Some deterioration of the image can be seen towards the left-hand side of the reconstruction area. This is due to the set of projection data from which the image is reconstructed being incomplete where there are portions of the patient outside the reconstruction area. The lead marker wires appear considerably larger than their actual size due to both the 2.3 mm pixel size (128 × 128 pixel image) and the point-spread effects generated within the imaging system. Streaking artefacts, although present, are not of

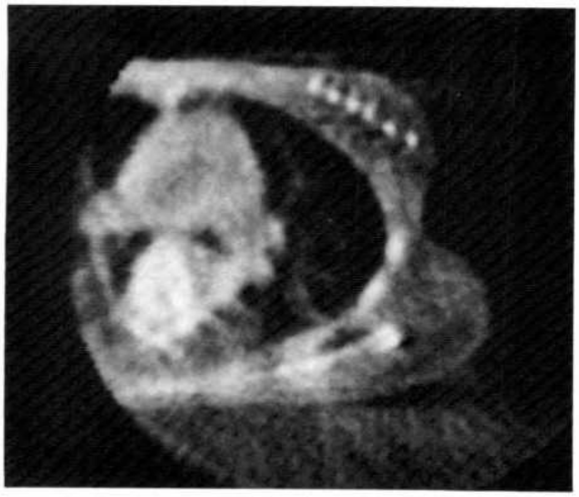

FIG. 1.

Simulator CT scan showing lead marker wires in the positions to be occupied by ^{192}Ir wire sources in a single-plane breast implant.

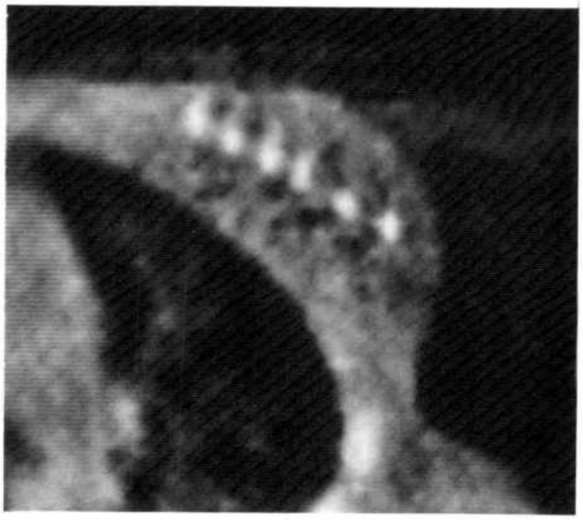

FIG. 2.

Digitally zoomed region of Fig. 1 showing just the breast and implant.

sufficient amplitude to affect interpretation. As well as video display, the image can be presented as a life-sized grey-scale print-out.

Source co-ordinate positions can be measured directly from the hard copy and are used in a simple in-house dosimetry program which ignores both absorption and scatter in tissue and oblique absorption within the wire (Casebow, 1984). Points for calculation of basal dose-rates are identified on the basis of the geometric principles of the Paris system (Pierquin et al, 1978) and the co-ordinates obtained by direct measurement from the hard copy. The mean of the basal dose-rates is used to obtain the reference dose-rate upon which the dose prescription for the implant is based.

A comparison of the overall width of implants assessed from both the CT print-out and the orthogonal radiographs using conventional calculation methods has shown excellent agreement, the maximum discrepancy in overall width being less than 2 mm. Where CT data prove particularly advantageous, however, is in the interpretation of implants where the spacing is uneven or the plane is curved, or in more complex multiplane implants. To obtain these data by purely conventional radiographic techniques is particularly difficult and time consuming. At our centre, before the use of simulator CT, the effect of uneven wire spacing tended to be ignored. Now it is a straightforward matter to take this into consideration and also to relate potential areas of high and low dose to the patient's anatomy as displayed on the simulator CT scan.

REFERENCES

CASEBOW, M. P., 1984. Dosimetry tables for standard iridium-192 wire planar implants. *British Journal of Radiology, 57,* 515–518.

KOTRE, C. J., HARRISON, R. M. & ROSS, W. M., 1984. A simulator-based CT system for radiotherapy treatment planning. *British Journal of Radiology, 57,* 631–635.

PIERQUIN, B., DUTREIX, A., PAINE, C. H., CHASSAGNE, D., MARINELLO, G. & ASH, D., 1978. The Paris system in interstitial radiation therapy *Acta Radiologica Oncology, 17,* 33–47.

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Case reports

Failure of radiotherapy to reverse progressive pulmonary fibrosis caused by paraquat

By *L. L. Bloodworth, M.R.C.P., †J. B. Kershaw, M.R.C.Path., P. E. Stevens, B.Sc., M.R.C.P., ‡C. J. Alcock, M.R.C.P., F.R.C.R. and D. J. Rainford, F.R.C.P.

Department of Renal Medicine, Princess Mary's RAF Hospital, RAF Halton, Aylesbury HP22 5PS, †Royal Air Force Institute of Pathology and Tropical Medicine, RAF Halton, Aylesbury HP22 5PG and ‡Department of Radiotherapy and Oncology, The Churchill Hospital, Oxford OX3 7LJ

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Pulmonary fibrosis following poisoning by paraquat almost invariably proves fatal. A recent case report suggested that the pulmonary damage might be reversed by whole-lung irradiation (Webb et al, 1984). We describe a patient whom we treated in a similar manner, without success.

CASE REPORT

A student aged 20 years was admitted approximately 3 h after deliberate ingestion of 50–100 ml of Gramoxone (containing 10–20 g of paraquat). Stomach wash-out was performed on admission. He was then treated with Fuller's earth and an oral mannitol purge; 7.5 h after ingestion, the plasma paraquat was 980 μg/l. At 36 h after ingestion he was transferred to our care for charcoal column haemoperfusion (CHP). He was drowsy and unwell with gross oro-pharyngeal ulceration and a temperature of 38.0°C. His chest was clinically clear and there were no other abnormal findings. During CHP, flow rates of 250 ml/min were achieved with a prostacyclin and heparin infusion for anticoagulation. Paraquat levels were 120 μg/l and 90 μg/l pre- and 6 h post-perfusion, respectively.

On Day 4 he developed right interstitial lung shadowing with an arterial pO_2 of 12.4 kPa. A 1 g bolus of intravenous methylprednisolone was given, followed by prednisolone 60 mg/day and cyclophosphamide 100 mg/day. The next day there was radiographic deterioration involving both lungs with a decline in arterial oxygen tension ($pO_2 = 8.49$ kPa) and radiotherapy was commenced (Webb et al, 1984). Both lungs were irradiated with parallel opposed anterior and posterior portals, on a cobalt unit. A midline dose of 1100 cGy (rad), without lung correction, was administered in five daily fractions. This dosage scheme was chosen to be comparable with that described in the paper by Webb et al.

On Day 6 he required mechanical ventilation because of increasing hypoxia. Low inspired oxygen tension with positive end-expiratory pressure was employed to minimise pulmonary oxygen toxicity. Subsequent chest radiographs revealed progressive pulmonary shadowing with associated difficulty in maintaining adequate oxygenation. The patient died of pulmonary failure on Day 23. Post-mortem examination revealed pulmonary changes characteristic of paraquat poisoning (Rebello & Mason, 1978). The lungs weighed in excess of 2 kg with bosselated surfaces and a rubbery consistency. The cut surfaces showed areas of honeycombing, consolidation and focal areas of bronchiectasis. Microscopically there was severe diffuse intra-alveolar haemorrhage and fibrosis. Interstitial fibrosis was prominent in a focal distribution and areas of epithelial proliferation were present (Figs 1 and 2).

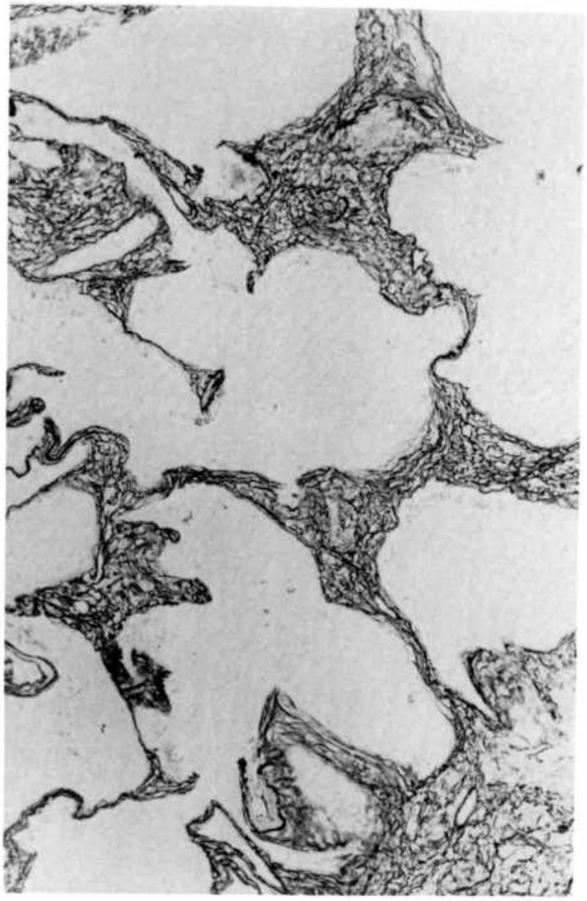

FIG. 1.

A section of lung showing interstitial fibrosis with honeycombing. Reticulin, × 275 (including print magnification).

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*Author for correspondence.

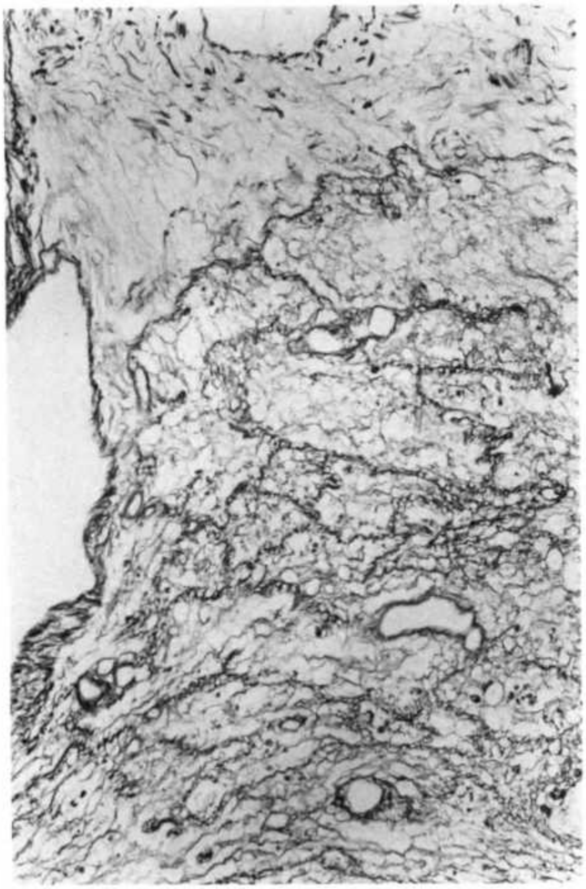

FIG. 2.

Intra-alveolar fibrosis with obliteration of air spaces against a background outline of alveolar walls. Reticulin, ×275 (including print magnification).

DISCUSSION

This patient differs from that described by Webb et al in the severity of poisoning (10–20 g of ingested paraquat in our case versus 3 g in Webb's case) and this was reflected in the more acute development of lung toxicity, mechanical ventilation being required in under 6 days from ingestion in our case. The paraquat level at 36 h (120 μg/l) was not dissimilar to Webb's patient (80 μg/l), however, by this time a considerable proportion of the absorbed paraquat would have been tissue-fixed and hence plasma levels are a poor index of the severity of poisoning. In terms of clinical management, as summarised in Fig. 3, the cases were otherwise similar. Both patients received steroids and cyclophosphamide, although our patient received an additional 1 g bolus of methylprednisolone at the onset of radiological shadowing and a lower dose of cyclophosphamide (1.5 mg/kg versus 3 mg/kg in Webb's case). Both patients received CHP at approximately the same time into their illness. The more severe respiratory embarrassment of the patient described precluded either an open or transbronchial lung biopsy to determine if fibroblast proliferation was occurring at the time of irradiation.

The initial plasma paraquat level indicated a 30–50% survival probability (Hart et al, 1984) and the addition of radiotherapy did not favourably influence the outcome. Indeed, it has to be considered whether irradiation of the lungs at this time can increase the damage to the lung parenchyma. Recently published work on the effect of radiotherapy in mice poisoned with paraquat does little to allay these fears (Parkins & Fowler, 1985). The treatment of an extremely sick ventilated patient with radiotherapy poses major logistic difficulties and may necessitate the daily transfer of the patient to a radiotherapy unit which may be some distance away, with the attendant risk to the

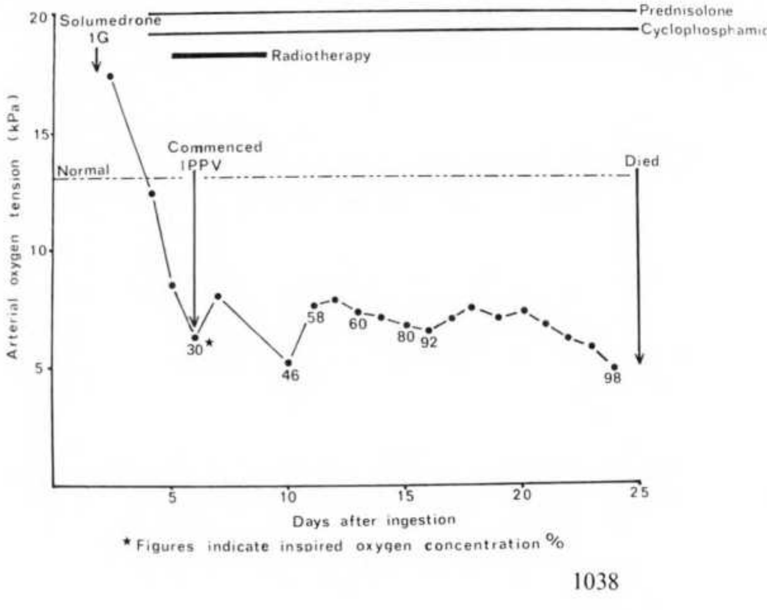

FIG. 3.

Summary of clinical course and treatment given.

patient that such moves may entail.

In conclusion, the addition of radiotherapy in the treatment of paraquat lung in this patient did not lead to the dramatic improvement in pulmonary damage as seen in the case described by Webb et al (1984). It may be that less severe poisoning is more amenable to treatment (Williams et al, 1985), but clearly more research is required to determine the place, if any, of radiotherapy in the management of paraquat poisoning.

REFERENCES

HART, T. B., NEVITT, A. & WHITEHEAD, A., 1984. A new statistical approach to the prognostic significance of plasma paraquat concentrations. *Lancet*, *ii*, 1222–1223.

PARKINS, C. S. & FOWLER, J. F., 1985. A cautionary note on the resolution of paraquat lung damage after radiotherapy. *British Journal of Radiology*, *58*, 1137–1140.

REBELLO, G. & MASON, J. K., 1978. Pulmonary histological appearances in fatal paraquat poisoning. *Histopathology*, *2*, 53–56.

WEBB, D. B., WILLIAMS, M. V., DAVIES, B. H. & JAMES, K. W., 1984. Resolution after radiotherapy of severe pulmonary damage due to paraquat poisoning. *British Medical Journal*, *288*, 1259–1260.

WILLIAMS, M. V., WEBB, D. B., JAMES, K. W. & DAVIES, B. H., 1985. Lung irradiation for paraquat toxicity. *British Journal of Radiology*, *58*, 1144.

Radiation reaction enhanced by ifosfamide

By J. J. Nicoll, M.A., M.R.C.P.

Stanford Cade Department of Clinical Oncology, Westminster Hospital, Horseferry Road, London SW1P 2AP

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Ifosfamide is a relatively new cytotoxic drug with activity against many tumours including oat-cell lung cancer (Haggard, 1967), ovarian cancer (De La Garza & Cardenas, 1982), testicular tumours (Schmoll, 1982), osteosarcoma (Marti et al, 1981), soft-tissue sarcoma (Czownicki & Utracka, 1982; Stuart-Harris et al, 1983) and Hodgkin's lymphoma (Czownicki & Utracka-Hutka, 1977). Because of its activity in soft-tissue sarcoma we have used it in combination with radiotherapy as primary treatment for this condition. We report a case in which the combination of ifosfamide and radiation led to an enhanced radiation reaction.

CASE REPORT

A 33-year-old soldier presented with cough, low back pain radiating into the left buttock and a swelling over the left sacro-iliac joint. Examination showed a bony, hard lump arising from the region of the left sacro-iliac joint and computed tomography showed a large tumour eroding the lower lumbar vertebrae and invading the pelvis through the greater sciatic notch. Needle biopsy showed a poorly differentiated chondrosarcoma.

The tumour was considered inoperable and it was decided to treat it with radiotherapy and ifosfamide. Radiation was commenced on April 6, 1985, using a 5 MeV linear accelerator to deliver 200 cGy daily to the tumour volume through opposing tangential ports measuring 26 cm × 15 cm. The total tumour dose was 5640 cGy delivered in 29 fractions over 63 days, and the maximum skin and tissue doses were 7020 cGy (250 cGy daily). Ifosfamide, 5 g/m^2, was given 1 week before irradiation and repeated at 3-weekly intervals to a total of six courses, three of which were given during the course of radiotherapy. Mesna was given in standard doses.

On Day 26 of the treatment, at a tumour dose of 3200 cGy (maximum skin dose 4000 cGy), a macular rash was noticed over the whole treatment area and within a week this had developed into the most severe moist desquamation (Fig. 1). The reaction was confined to the skin of the exit ports and was so severe that irradiation had to be interrupted for 2 weeks to allow some healing to take place. Thereafter, radiotherapy was continued with small fractions of 180 cGy daily to the tumour volume (225 cGy maximum daily skin dose).

After the completion of radiotherapy and the healing of the acute reaction the skin gradually became hyperpigmented and leathery. Six months later the whole treatment area, including the skin and deep subcutaneous tissues, was so severely fibrosed as to be almost woody to touch. The skin was deep

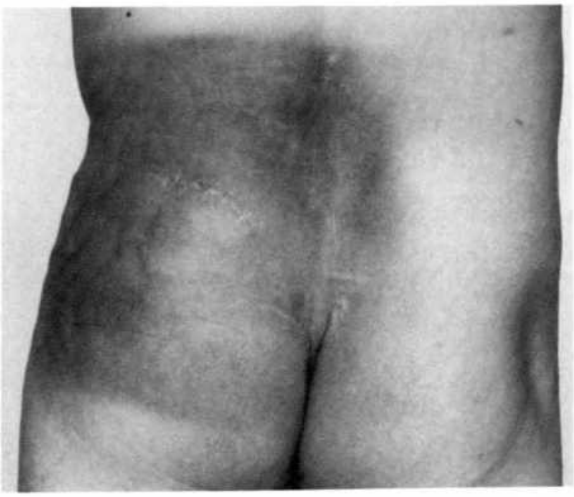

FIG. 1.

Severe moist desquamation of the skin occurring during a course of combined radiotherapy and ifosfamide.

red in colour and the induration so great that it was impossible to move the skin or subcutaneous tissue at all. A year after primary treatment there has been no change in this woody appearance.

The primary tumour regressed during radiotherapy and there is no sign of recurrence 1 year later. Eight months after the initial treatment the patient received localised irradiation to metastases to the lungs. No abnormal radiation reaction was seen on this occasion.

Discussion

Cytotoxic drugs are used in conjunction with radiotherapy both to kill cells outside the target volume and to enhance cell kill within the target volume (Steel & Peckham, 1979). Although the role of adjuvant chemotherapy in the management of soft-tissue sarcoma is not clear (Edmonson, 1984), numerous trials of combined-modality therapy have been carried out (Daly & Friedman, 1974; Silverberg et al, 1976; Bleehen, 1979; Ryall et al, 1979; Sealy, 1979; Spittle et al, 1979; Urtasun et al, 1982; Von Der Maase et al, 1982).

Because the major toxicity of ifosfamide can be controlled (Scheulen et al, 1983a, b), it is an attractive drug for use in an adjuvant setting. We have, therefore, also used ifosfamide in conjunction with radiotherapy after surgical removal of pulmonary metastases for soft-tissue sarcoma and because of our experience with this patient we believe there is a possibility that the combination of ifosfamide and pulmonary irradiation may lead to pulmonary fibrosis. That pulmonary fibrosis was not seen in our patient is probably because of the time interval between ifosfamide and irradiation and the small volume irradiated.

It is well known that interaction of radiotherapy and cytotoxic drugs may lead to increased toxicity (Berry, 1982), the common pattern being of a radiation reaction enhanced by concurrent administration of cytotoxic agent. Drugs for which such interaction have been described are methotrexate (Friedman & Daly, 1967), bleomycin (Lindholm et al, 1980; Catane et al, 1980; Shanta & Krishnamurthi, 1976), etoposide (Giever et al, 1981), Adriamycin (Farmitalia C. E. Ltd, St Albans) (Mayer et al, 1976; Aristizabal et al, 1977; Kinsella et al, 1979), razoxane (Spittle et al, 1979) and actinomycin D (D'Angio, 1962).

This is the first report of skin damage caused by an interaction between ifosfamide and radiation. Because of the very severe acute skin reaction and the late woody fibrosis seen in this patient we no longer administer ifosfamide during a course of radiotherapy.

Acknowledgments

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REFERENCES

Aristizabal, S. A., Miller, R. C., Schlichtemeier, A. L., Jones, S. E. & Boone, M. L. M., 1977. Adriamycin-irradiation cutaneous complications. *International Journal of Radiation Oncology, Biology, Physics*, *2*, 325–331.

Berry, R. J., 1982. Interaction of drugs and radiation—promise or pitfall? *Clinical Radiology*, *33*, 121–129.

Bleehen, N. M., 1979. Role of radiation therapy and other modalities in the treatment of small cell carcinoma of the lung. In *Lung Cancer: Progress in Therapeutic Research*, pp. 567–574.

Catane, R., Schwade, J. G., Turrisi, A. T., Webber, B. L. & Muggia, F. M., 1980. *Pulmonary Toxicity After Radiation and Bleomycin. A Review.* Cancer Therapy Evaluation Program, and Radiation Oncology Branch, Clinical Oncology Program, Division of Cancer Treatment, National Cancer Institute.

Czownicki, Z. & Utracka, B., 1982. Ifosfamide (Holoxan) single-agent therapy in soft tissue sarcomas: a clinical phase II study. *Proceedings of the 13th International Cancer Congress, Seattle*, (Abstract 2379), p. 416.

Czownicki, Z. & Utracka-Hutka, B., 1977. Contribution to the treatment of malignant tumours with Ifosfamide. *Proceedings of the International Holoxan Symposium, Dusseldorf.* Bielefeld. Asta-Werke, 109–111.

Daly, J. & Friedman, M., 1974. Combined irradiation and chemotherapy in the treatment of squamous cell carcinoma of the head and neck. *Transactions of the American Academy of Ophthalmology and Otolaryngology*, *68*, 625–643.

D'Angio, G. J., 1962. Clinical and biologic studies of Actinomycin D and Roentgen irradiation. *American Journal of Roentgenology, Radium Therapy and Nuclear Medicine*, *87*, 106–109.

De la Garza, J. & Cardenas, J., 1982. Ifosfamide (Holoxan, IFA) in the treatment of advanced ovarian carcinoma. *Proceedings of the 13th International Cancer Congress, Seattle*, (Abstract 428), p. 76.

Edmonson, J. H., 1984. Role of adjuvant chemotherapy in the management of patients with soft tissue sarcomas. *Cancer Treatment Reports*, *68*, 1063–1066.

Friedman, M. & Daly, J. F., 1967. The treatment of squamous carcinoma of the head and neck with Methotrexate and irradiation. *American Journal of Roentgenology*, *99*, 281–301.

Giever, R. J., Heusinkveld, R. S., Manning, M. R. & Bowden, G. T., 1981. Enhanced radiation reaction following combination chemotherapy for small cell carcinoma of the lung, possibly secondary to VP16–213. *International Journal of Radiation Oncology, Biology, Physics*, *8*, 921–923.

Haggard, M. E., 1967. Cyclophosphamide (NCS-2627) in the treatment of children with malignant neoplasms. *Cancer Chemotherapy, Report 51*, 403.

Kinsella, T. J., Ahmann, D. L., Guiliani, E. R. & Lie, J. T., 1979. Adriamycin cardiotoxicity in stage IV breast cancer: possible enhancement with prior left chest radiation therapy. *International Journal of Radiation Oncology, Biology, Physics*, *5*, 1997–2002.

Lindholm, C., Littbrand, B. & Lofroth, P. O., 1980. Superfractionated irradiation combined with low doses of Bleomycin in the treatment of oral carcinoma. *Acta Radiologica*, *19*, 417–420.

Marti, Ch., Kroner, Th. & Cserhati, M., 1981. Ifosfamide in the treatment of refractory metastatic osteosarcoma. UICC-Congress 1981, Lausanne (Abstract 05-0041)

Mayer, E. G., Poulter, C. A. & Aristizabal, S. A., 1976. Complications of irradiation related to apparent drug potentiation by Adriamycin. *International Journal of Radiation Oncology, Biology, Physics*, *1*, 1179–1188.

Ryall, R. D. H., Bates, T., Newton, K. A. & Hellmann, K., 1979. Combination of radiotherapy and Razoxane (ICRF 159) for chondrosarcoma. *Cancer*, *44*, 891–895.

1986, *The British Journal of Radiology*, *59*, 1041–1043 OCTOBER 1986

SCHEULEN, M. E., BREMER, K., NIEDERLE, N. & SEEBER, S., 1983a. Treatment of refractory malignant lymphomas with Ifosfamide/Etoposide combination chemotherapy. *Cancer Treatment Reviews*, *10*, 137–143.

SCHEULEN, M. E., NIEDERLE, N., BREMER, K., SCHUTTE, J. & SEEBER, S., 1983b. Efficacy of Ifosfamide in refractory malignant diseases and uroprotection by Mesna: results of a clinical phase II-study with 151 patients. *Cancer Treatment Reviews*, *10*, 93–101.

SCHMOLL, H. J., 1982. The role of Ifosfamide (IPP) in testicular cancer. *Proceedings of the 13th International Cancer Congress, Seattle* (Abstract 3580), p. 626.

SEALY, R., 1979. Combined radiotherapy and chemotherapy in non-small cell carcinoma of the lung. In *Lung Cancer: Progress in Therapeutic Research*, 315–323.

SHANTA, V. & KRISHNAMURTHI, S., 1976. The combined therapy of oral cancer. *Gann Monograph on Cancer Research*, *19*, 159.

SILVERBERG, I. J., PHILLIPS, T. L., FU, K. & CHAN, Y. M., 1976. Bleomycin with radiation therapy in the treatment of head and neck malignancies. *Proceedings of the American Association for Cancer Research and American Association of Clinical Oncology*, *17*, 279.

SPITTLE, M. F., BUSH, H., JAMES, S. E. & HELLMANN, K., 1979. Clinical trial of Razoxane and radiotherapy for inoperable carcinoma of the bronchus. *International Journal of Radiation Oncology, Biology, Physics*, *5*, 1649–1651.

STEEL, G. G. & PECKHAM, M. J., 1979. Exploitable mechanisms in combined radiotherapy-chemotherapy: the concept of additivity. *International Journal of Radiation Oncology, Biology, Physics*, *5*, 85–91.

STUART-HARRIS, R., HARPER, P. G., KAYE, S. B. & WILTSHAW, E., 1983. High-dose Ifosfamide by infusion with Mesna in advanced soft tissue sarcoma. *Cancer Treatment Reviews*, *10*, 163–164.

URTASUN, R., FELDSTEIN, M. L., PARTINGTON, J., TANASICHUK, H., MILLER, J. D. R., RUSSELL, D. B., AGBOOLA, O. & MIELKE, B., 1982. Radiation and nitroimidazoles in supratentorial high grade gliomas: a second clinical trial. *British Journal of Cancer*, *46*, 101–108.

VON DER MAASE, H., MAGNUSSON, K. & SVEINSSON, T., 1982. Combined irradiation and three-drug chemotherapy in inoperable colorectal carcinoma. *Acta Radiologica*, *21*, 369–372.

Ultrasound appearances of peripheral nerve tumours

By David G. Hughes, M.R.C.P. and *David J. Wilson, M.R.C.P., F.R.C.R.

Department of Radiology, Nuffield Orthopaedic Centre, Headington, Oxford

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Diagnostic ultrasound is well established as an imaging modality for identifying peripheral soft-tissue masses (Bernardino et al, 1981; Bluth et al, 1982). However, little has been reported about the ultrasound appearances of peripheral nerve tumours; we could find only two case reports (Chinn et al, 1982; Reuter et al, 1982). We present three patients with peripheral nerve tumours, all with similar ultrasound appearances.

CASE REPORTS

Case 1

A 68-year-old woman had a history of a lump in the right popliteal fossa for 3 years. This had been slowly increasing in size and had recently become painful. Palpation revealed a 2 cm lesion in the midline and produced pain radiating down to the instep. Real-time (Fig. 1) and B-mode ultrasonography showed a clearly defined rounded mass 1.5 cm in diameter. There were low levels of echo within the lesion and moderate distal acoustic enhancement. At surgery, a well defined mass related to the popliteal nerve was removed. Histology showed this to be a schwannoma.

Case 2

A 34-year-old man had had a schwannoma resected from the sole of his foot in 1968. Regrowths occurred in 1977 and 1979 and were locally resected. In 1985 there was a further recurrence. This was imaged with real-time ultrasound. The appearances were of a mass of low echogenicity with some distal acoustic enhancement (Fig. 2). Histology proved this to be a neurofibrosarcoma.

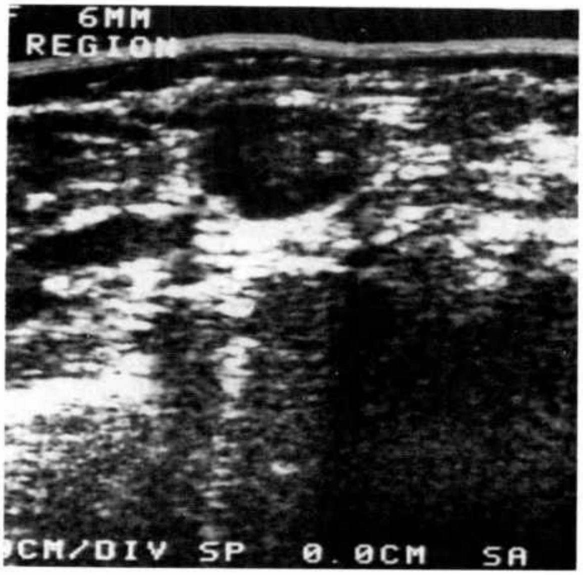

FIG. 1. *Case 1.*

10 MHz real-time scan showing low levels of echo within the schwannoma.

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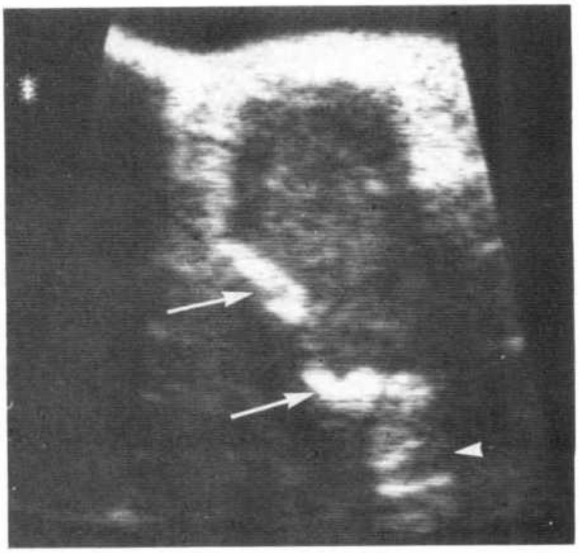


FIG. 2. *Case 2.*

Area of reduced echogenicity of neurofibrosarcoma. White arrows point to complete reflection of sound by tarsal bones and white arrowhead to the area of acoustic enhancement.

Case 3

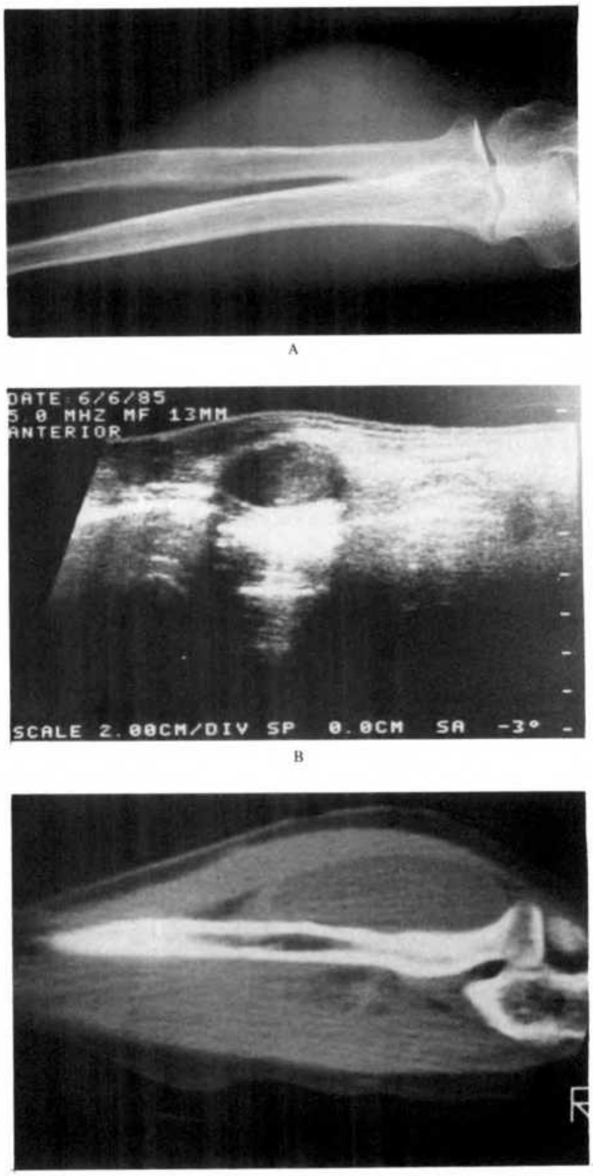
A 52-year-old woman, who was known to have neurofibromatosis, had noticed a swelling in the right side of her forearm for 6 months. On palpation, there was a firm, non-tender swelling in the region of the common extensor origin of the right arm and clinical suspicion of malignant change. Ultrasound showed a mass of low echogenicity with marked posterior acoustic enhancement and clearly defined borders (Fig. 3A, B). This was confirmed by computed tomography (Fig. 3C). A 6 cm-diameter tumour associated with the posterior interosseous nerve was removed at surgery. Histology proved this to be a benign neurofibroma.

DISCUSSION

All three tumours had similar ultrasound appearances of an echo-poor mass with distal acoustic enhancement. Not surprisingly, the neurofibrosarcoma had less well defined margins. Of the two other reported cases, the schwannoma discussed by Chinn et al (1982) showed these features, although the neurofibroma discussed by Reuter et al (1982) had only poor back-wall enhancement.

The mechanism for this appearance (discussed by Chinn et al) seems likely to be due to the sound attenuation of neurinomas being lower than the surrounding muscle. We recommend comparison with a known area of fluid, such as the urinary bladder, as low level echoes in the mass may be obliterated by an inappropriately low gain setting.

Our cases emphasise that solid, soft-tissue masses of neural origin may present with ultrasonic appearances suggestive of a fluid-filled cyst (Callen & Marks, 1979). We conclude that this may be the normal ultrasound appearance of peripheral nerve tumours.



A

B

C

FIG. 3. *Case 3.*

(A) Radiograph of the soft-tissue mass. (B) B-mode ultrasound scan showing marked posterior echo enhancement. (C) Computed tomograph of the soft-tissue mass.

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REFERENCES

BERNARDINO, M. E., BAO-SHAN JING, THOMAS, J. L., LINDELL, M. M. & ZORNAOZA, J., 1981. The extremity soft-tissue lesion: a comparative study of ultrasound, computed tomography and xeroradiography. *Radiology*, *139*, 53–59.

BLUTH, E. I., MERRITT, C. R. B. & SULLIVAN, M. A., 1982. Gray-scale ultrasound evaluation of the lower extremities. *Journal of the American Medical Association*, *247*, 3127–3129.

CALLEN, P. W. & MARKS, W. M., 1979. Lymphomatous masses simulating cysts by ultrasonography. *Journal of the Canadian Association of Radiology*, *30*, 244.

CHINN, D. H., FILLY, R. A. & CALLEN, P. W., 1982. Unusual ultrasonographic appearance of a solid schwannoma. *Journal of Clinical Ultrasound*, *10*, 243–245.

REUTER, K. L., RAPTOPOULOS, V., DE GIROLAMI, U. & AKINS, C. M., 1982. Ultrasonography of a plexiform neurofibroma of the popliteal fossa. *Journal of Ultrasound in Medicine*, *1*, 209–211.

Simple procedure for the removal of a non-deflating balloon bladder catheter: two cases

By T. C. Naunton Morgan, F.R.C.S., N. K. Barrett, M.R.C.P. and J. E. Boultbee, F.R.C.R.

Department of Radiology, Charing Cross Hospital, Fulham Palace Road, London W6 8RF

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The occurrence of a non-deflating balloon catheter in the bladder is uncommon (Higgins & Mace, 1984). When all other routine urological methods of deflating the balloon have failed (Pitt, 1970) the aid of the radiologist should be sought so as to perform percutaneous balloon puncture (Rees & Joseph, 1981).

We report two patients, who presented to our hospital within 10 days of each other, for whom initial attempts at deflating the balloons had been unsuccessful.

CASE REPORTS

Case 1

A 61-year-old hemiplegic male with a long-term, self-retaining balloon catheter which had become completely obstructed presented to our hospital. Attempts to free the obstruction were unsuccessful and it was therefore decided to remove the catheter. Unfortunately, the balloon could not be deflated and the urologists were asked for their advice. Despite cutting the side-tube and instilling ether, the balloon remained inflated. The patient's discomfort increased and urgent remedial treatment was considered necessary. It was felt that open cystotomy, being a major procedure, should not be undertaken lightly, and so the patient was referred to the X-ray department for ultrasound-guided puncture of the balloon (Rees & Joseph, 1981).

Using a Diasonics DRF 400 real-time scanner, the intravesical balloon was easily localised in a full bladder (Fig. 1). A 10 ml aliquot of 2% lignocaine was infiltrated into the suprapubic region above the balloon. Under full sterile conditions and using sterile ultrasonic gel, a 22-gauge disposable needle was inserted into the bladder under direct ultrasound control. The tip was manoeuvred so that it lay directly over the balloon and while traction was applied to the catheter, the balloon was punctured with an audible "pop", its destruction being dramatically displayed on the ultrasound screen. The catheter was then removed.

Case 2

The second patient was a 64-year-old post-laryngectomy patient who had been catheterised for post-operative retention. The balloon could not be deflated, and so the urologist's opinion was sought. Despite repeating the antideflating manoeuvres, the balloon remained inflated and our help was requested.

The partially inflated balloon was seen to be lying with its distal end impacted in the prostatic urethra. It was not possible to re-introduce the balloon into the bladder and we were unable to distend the balloon further as the side-channel had been damaged. We did, however, fill the bladder to make the puncture easier. Using local anaesthesia and a strictly aseptic technique, a 22-gauge needle was inserted but, because of the needle's flexibility and the position of the inflated balloon, it was technically difficult to visualise the needle tip and guide it into the prostatic urethra. We therefore changed to a 16-gauge Abocath needle with a plastic sheath around the central stilette. This was much more rigid and more easily visible. Despite the slightly larger size of the Abocath needle, the patient experienced no great discomfort with adequate local anaesthesia. Balloon puncture was then performed and the catheter removed.

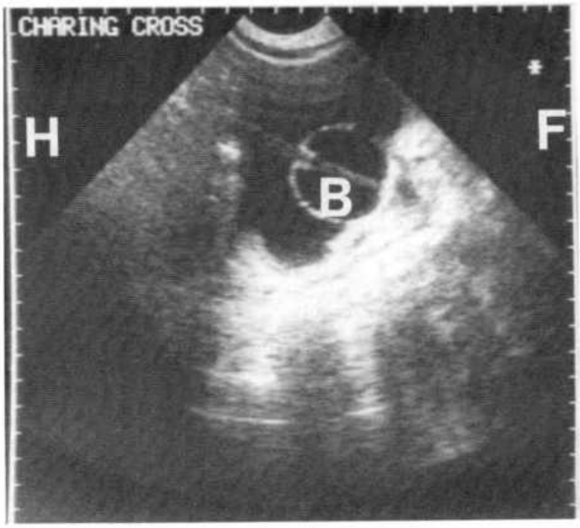

FIG. 1.

Longitudinal scan through the bladder: H indicates cephalad, F indicates caudad and B indicates inflated balloon in bladder.

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DISCUSSION

Numerous methods have been advocated for puncturing non-deflating balloons and methods included instillation of ether down the balloon-filling channel (Pitt, 1970) and blind suprapubic puncture with a lumbar puncture needle (Moskovich, 1984). Ether, which was widely used, is falling into disrepute because of the risk of cystourethritis and retained balloon fragments. Another method of puncturing the balloon is to insert the stilette of a ureteric catheter into the balloon channel, after severing the valve, and advance it until it reaches the balloon (Sood & Sahota, 1972). This procedure failed in both patients.

A cystogram can be performed to localise the balloon within the bladder (Moisey & Williams, 1980). However, the use of X rays is unnecessary for this procedure, as the balloon can be adequately visualised by ultrasound, without using ionising radiation (Higgins & Mace, 1984).

We feel that ultrasound-guided suprapubic puncture of the balloon, under strict asepsis and local anaesthesia, is a rapid, simple, safe manoeuvre which is easy to perform and which does not run the risk of a chemical cystitis, retained products in the bladder or the trauma caused by a blind suprapubic stab or the blind insertion of a ureteric stilette down the filling channel. In view of our success, urologists will, in future, be referring patients directly to us if the balloon catheter does not deflate spontaneously.

REFERENCES

HIGGINS, W. L. & MACE, A. H., 1984 Puncture of a non-deflatable Foley balloon using ultrasound guidance *Radiology*, *151*, 801.

MOISEY, C. U. & WILLIAMS, L. A., 1980. Self-retained balloon catheters—a safe method for removal. *British Journal of Urology*, *52*, 67.

MOSKOVICH, R., 1984. Suprapubic puncture for non-deflating urethral balloon catheters. *Journal of the Royal College of Surgeons of Edinburgh*, *29*, 181–183.

PITT, P. C. C., 1970. Self-retained catheter. *British Journal of Hospital Medicine*, *4*, 174.

REES, M. & JOSEPH, A. E. A., 1981 Ultrasound guided suprapubic puncture—a new, simple way of releasing a blocked Foley balloon. *British Journal of Urology*, *53*, 196.

SOOD, S. C. & SAHOTA, H., 1972. Removing obstructed balloon catheter. *British Medical Journal*, *4*, 735

Ultrasound used to detect a stone in the vesico-ureteric junction during pregnancy

By G. Rubin, B.Sc., F.R.C.R. and *P. J. Fitzsimons, M.B., D.M.R.D., F.F.R.R.C.S.I.

Department of Radiology, the Whittington Hospital, London N19

(*Received December 1985*)

Renal colic is conventionally diagnosed by a plain abdominal radiograph and intravenous urography. The role of ultrasound is controversial as it is only recently that it has imaged normal ureters (Marchal et al, 1982) and has detected stones in the lower ureter and in the vesico-ureteric junction (Erwin et al, 1984). We report a case of a pregnant woman where ultrasound replaced other imaging techniques in detecting a stone in this region.

CASE REPORT

A 32-year-old woman who was 11 weeks pregnant presented with left renal colic. Ultrasound demonstrated a hydronephrotic left kidney and a normal right kidney. The left vesicoureteric junction was then examined by identifying the urethra on a transverse caudally angled scan of the bladder. Maintaining a transverse plane, the transducer was angled cranially until the vesico-ureteric junction with an impacted stone was identified (Fig. 1). The transducer was then rotated obliquely by 70° giving a semilongitudinal view of the dilated left lower ureter (Fig. 2) entering the bladder, allowing a diagnosis of a ureteric calculus to be made.

DISCUSSION

Ultrasound can reliably detect hydronephrosis (Jeffrey & Federle, 1983) and stones in the kidney and bladder. It is superior to intravenous urography in diagnosing non-radiopaque renal stones (Pollack et al, 1978). However, its role in renal colic has been limited, because its ability to image calculi in ureters has not been fully appreciated, even though ultrasound has detected stones in the upper and lower thirds of the ureter (Erwin et al, 1984). As stones most frequently lodge in the distal ureter (Rous, 1981), this area must be specifically examined. The technique for this has been described by Marchal et al (1982) who saw at least one lower ureter even in normal subjects, and especially in paediatric practice this area is routinely examined for dilated lower ureters (Cremin, 1985). Visualisation requires a full bladder and, where this can be obtained, ultrasound has been useful in conjunction with a plain

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Correspondence to: Dr G. Rubin, X-ray Department, The Royal Free Hospital, Pond Street, London NW3 2QG.

*Present address. X-ray Department, University of Queensland, Royal Brisbane Hospital, Brisbane, Australia 4029

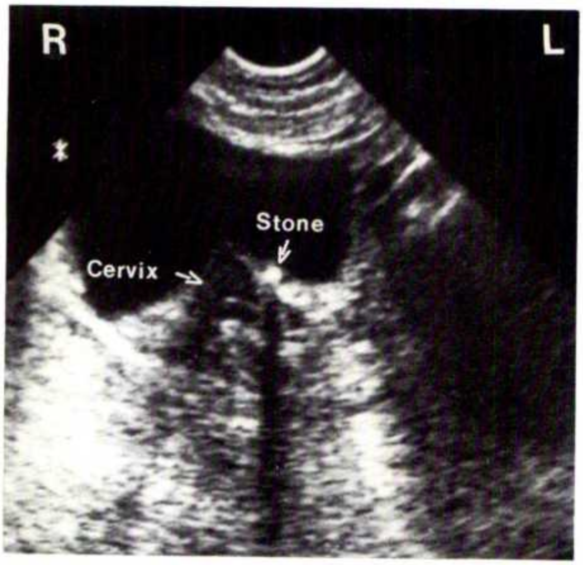

Fig. 1.

Transverse scan through the lower bladder showing a stone in the region of the left vesico-ureteric junction.

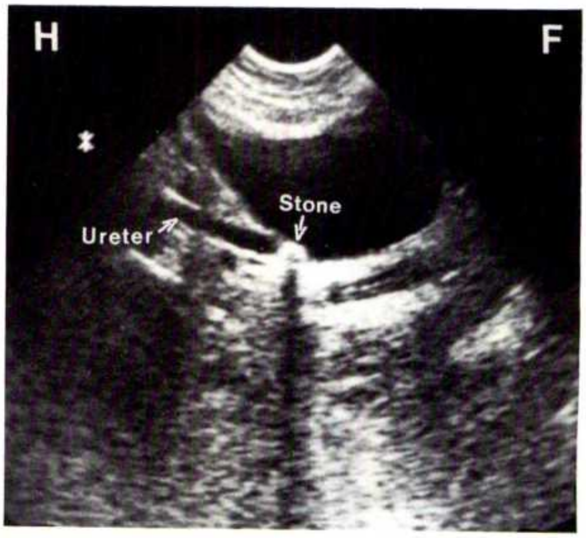

Fig. 2.

Oblique, semilongitudinal scan showing the dilated left ureter entering the bladder and confirming that the stone lies in the left vesico-ureteric junction. Note acoustic shadowing.

abdominal radiograph in evaluating renal colic and confirming stones in this region (Erwin et al, 1984). Where the bladder has not been full, ultrasound in renal colic has been disappointing (Laing et al, 1985).

Renal colic is fairly rare in pregnancy. Strong et al (1978) quote papers giving an incidence of between one in 286 and one in 3800. Ultrasound is the preferred imaging technique for investigating both pathological and physiological changes in the renal tract during pregnancy. Yet there is only one previous report of its use in renal colic where it showed a left-sided hydronephrosis. A plain abdominal radiograph showed a stone (confirmed at lithotomy) in the line of the left ureter, so intravenous urography was avoided (Broaddus et al, 1982). However, hydronephrosis in itself, especially in late pregnancy, particularly on the right, is unreliable as it occurs physiologically. Fortunately, calculi appear to be more common on the left (Strong et al, 1978).

The exact role of ultrasound in the routine investigation of suspected renal colic has not yet been defined. However, in patients who are also pregnant it is the best initial investigation and can replace other investigations, if, as in our case, the obstructing stone can be detected. If the stone is in the distal ureter a full bladder is required.

REFERENCES

Broaddus, S. B., Catalano, P. M., Leadbetter, G. W., Jr & Mann, L. I., 1982. Cessation of premature labour following removal of distal ureteral calculus. *American Journal of Obstetrics and Gynecology, 143*, 846–848.

Cremin, B. J., 1985. Real time ultrasonic evaluation of the paediatric abdomen: technique and anatomical variations. A personal view. *British Journal of Radiology, 58*, 859–868.

Erwin, B. C., Carroll, B. A. & Sommer, F. G., 1984. Renal colic: the role of ultrasound in initial evaluation. *Radiology, 152*, 147–150.

Jeffrey, R. B. & Federle, M. P., 1983. CT and ultrasound of acute renal abnormalities. *Radiological Clinics of North America, 21*, 515–525.

Laing, F. C., Jeffrey, R. B., Jr & Wing, V. W., 1985. Ultrasound versus excretory urography in evaluating acute flank pain. *Radiology, 154*, 613–616.

Marchal, G. J., van Dijck, X. M., Kint, E. J., Peeters, S. R., Baert, A. L. & Goddeeris, P., 1982. The sonographic visualisation of the vesico-ureteric junction. *Computertomographie, 2*, 62–67.

Pollack, H. M., Arger, P. H., Goldberg, B. B. & Mulholland, S. G., 1978. Ultrasound detection of non-opaque renal calcui. *Radiology, 127*, 233–237.

Rous, S. N., 1981. A review of 171 consecutive patients with urinary lithiasis. *Journal of Urology, 126*, 376–379.

Strong, D. W., Murchinson, R. J. & Lynch, D. F., 1978. The management of ureteral calculi during pregnancy. *Surgery, Gynaecology and Obstetrics, 146*, 604–608.

Book review

Merrill's Atlas of Radiographic Positions and Radiologic Procedures, 6th edit., 3 volumes. Ed. by P W. Ballinger, pp. 464+Glossary (Vol 1), 462+Bibliography (Vol. 2), 342+Bibliography (Vol. 3), 1986 (Blackwell Scientific, Oxford/CV Mosby, St Louis), £104.50.

This book is dedicated to describing both routine and specialised procedures in radiology. There are three volumes containing 2876 illustrations, including 11 in full colour.

Volumes 1 and 2 contain radiographic terminology, along with topographic and surface anatomy which introduces the reader to detailed descriptions of all routine radiographic and fluoroscopic procedures. These procedures are all well illustrated and encompass many pathological and trauma-induced conditions, covering the whole radiological spectrum.

A particularly useful feature is the evaluation criteria after each projection listing guidelines to determine the technical acceptability of each radiograph.

Volume 3 looks at specialised procedures. There are chapters on computed tomography, digital vascular imaging, positron emission tomography, ultrasound and magnetic resonance imaging, among others All discuss historical development, explain the principles and give examples of clinical applications, with frequent comparisons between the various techniques.

Excellent radiographs and xerograms illustrate a chapter on mammography A chapter on paediatric radiography covers not only the technical problems encountered when radiographing young children, but considers also the psychological approach and includes the very topical subject of child abuse. Another topical subject, quality assurance, is discussed at length and there is plenty of advice on test tools available for a successful quality assurance programme.

Criticisms are few and mainly trivial, relating particularly to American terminology and spelling, and also to the absence of typical exposure factors: important considerations for students when preparing for examinations. However, there can be nothing but praise for the technical content of this comprehensive volume, which is well bound and plentifully illustrated. In one or two instances the sharpness and contrast of the radiograph is lacking but this does not detract from the text.

The cost, £104.50, might determine whether it will actually replace K. C. Clark's *Positioning in Radiography* as the radiographer's "bible". Certainly, similarities exists between the *Atlas* and K. C. Clark's book, but the overall modern and updated approach of the *Atlas*, plus a wealth of information on interventional and other sophisticated, current trends in radiology make this book excellent value for money and justify the extra cost. To departments building up a library, buy the *Atlas*; you will not be disappointed. It will also prove a good investment to students embarking on a career in radiography. To radiographers already in possession of K. C. Clark's book: Volume 3 of the *Atlas*, if available separately, would keep you abreast of modern trends without incurring too much extra expense.

B. LOVELAND

1986, *The British Journal of Radiology*, 59, 1047–1049

Case of the month

A bulging eye

By J. Gholkar, M.R.C.P., F.R.C.R., J. P. R. Jenkins, M.R.C.P., D.M.R.D., F.R.C.R. and *T. Sekiya, M.D., F.J.B.R.

Department of Diagnostic Radiology, University of Manchester, Oxford Road, Manchester M13 9PT

(Received April 1986)

A 27-year-old man presented with a long history of left-sided proptosis. Decreased vision in this eye was detected at a school eye-test at the age of 5 years. Over recent years the patient reported further deterioration of vision, increasing proptosis and pain in the affected eye.

On examination, there was 4 mm of axial proptosis on the left. The vision in the left eye was 6/24 compared with 6/6 in the right eye. Full ocular movements were noted. Visual field testing revealed no significant abnormality and formal examination of the central nervous system was otherwise normal. Radiographs of the skull and orbits were performed; the 20° occipito-frontal view is illustrated (Fig. 1).

What does the radiograph show and what is your differential diagnosis?

What would be your next investigation?

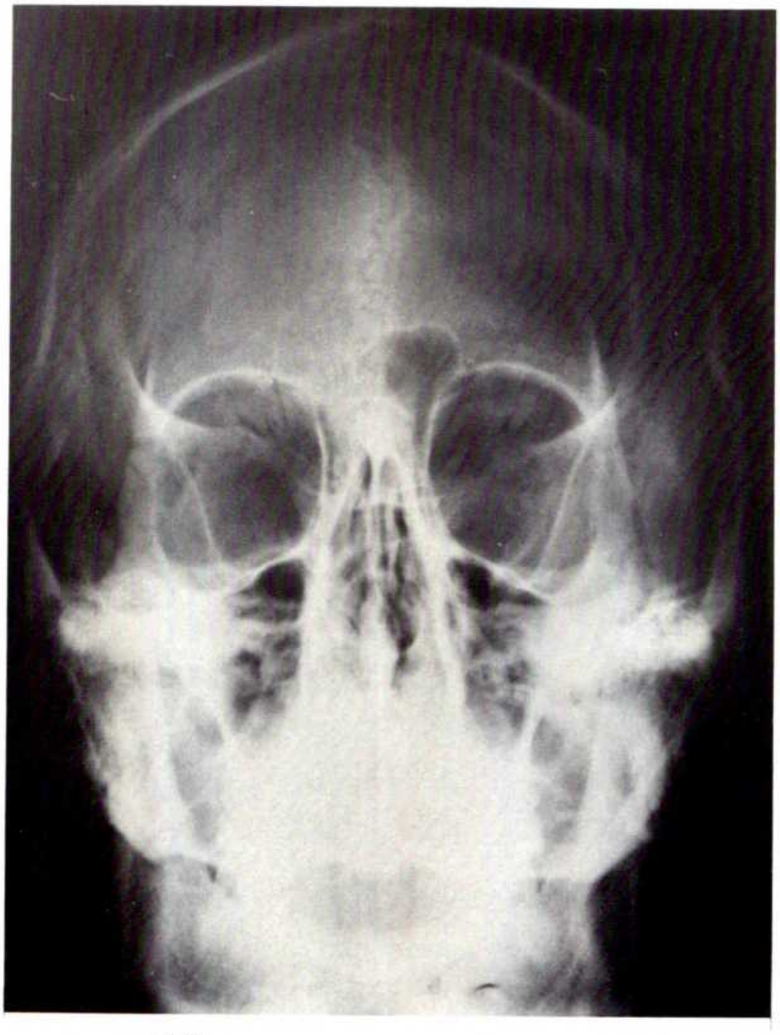

FIG. 1.
Plain radiograph taken at presentation.

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*Present address: Department of Radiology, The Jikei University School of Medicine, Tokyo, Japan.

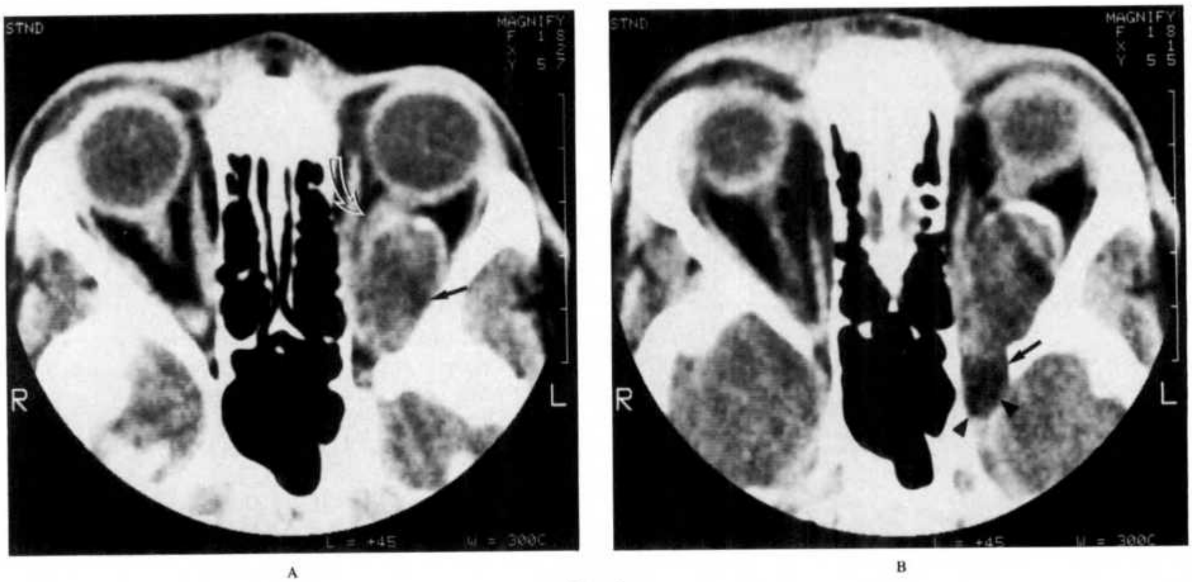

FIG. 2.

Two transverse CT scans through the orbits, (A) 3 mm inferior to (B). Note the large left intraconal tumour with calcification in its anterior wall and areas of low attenuation in keeping with fat (straight arrows). The medial displacement of the optic nerve (curved arrow in A) and the posterior extension of the tumour through the superior orbital fissure (arrowheads in B) are shown.

The radiograph shows widening of the left superior orbital fissure, which has a well defined rounded sclerotic margin. The pathological causes of this include (Lloyd, 1975):

(1) neurofibromatosis,
(2) metastasis to the wing of sphenoid,
(3) extension of orbital lesions, *e.g.* arteriovenous malformations, haemangioma, meningioma, dermoid, and
(4) extension of an intracranial lesion, *e.g.* meningioma, infraclinoid aneurysm, parasellar chordoma.

The long history and sclerotic margin in this case make a primary or secondary malignancy extremely unlikely and there were no other manifestations of neurofibromatosis.

A high-resolution computed tomogram of the orbits was the next investigation, and this showed a well defined tumour lying within the muscle cone of the left orbit, measuring approximately 4 cm × 2 cm × 2 cm. The tumour had a thin, partially calcified wall, contained areas of low attenuation (0 to −20 Hounsfield units) compatible with fat, and showed heterogeneous enhancement after intravenous contrast. The lesion was displacing the optic nerve medially (Fig. 2A); posteriorly it was expanding the superior orbital fissure and extended intracranially for approximately 1 cm (Fig. 2B).

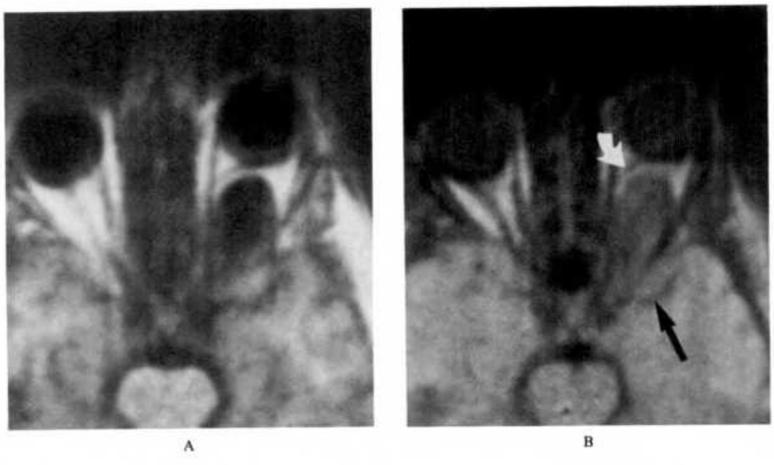

FIG. 3.

Two transverse MRI images at the same anatomical level through the orbit and tumour, (A) T_1-weighted (inversion recovery 1500/500) and (B) T_2-weighted (spin echo 1000/60). In (A) the tumour gives a low signal anteriorly (very long T_1) in keeping with a cyst. The posterior extent of the tumour through the superior orbital fissure has a shorter T_1 due to more solid elements. The medial displacement of the optic nerve is shown (curved arrow). The middle cerebral artery is undisplaced (straight arrow).

Magnetic resonance imaging (MRI) was also performed, at one anatomical level, through the orbits using a variety of T_1- and T_2-weighted pulse sequences and a back-projection method for image reconstruction. The site of the intraconal mass and associated displacement of surrounding structures were displayed. The lesion was well demarcated from surrounding retrobulbar fat on all sequences (Fig. 3). It had a well defined capsule and appeared cystic, with a very long T_1 relaxation time. The calcification within the wall of the lesion was not delineated on MRI because of poorer resolution for the detection of calcification compared with computed tomography (CT), and MRI added no extra useful information.

The diagnosis was made of an intraconal dermoid because of the well defined nature of the lesion, calcification in its rim and areas of fat. The tumour was excised and was shown to be an epidermoid cyst on histology.

Sequestration dermoids and epidermoids are formed when dermal or epidermal elements become pinched off along one of the lines of fusion in the course of embryonic development. They contain varying amounts of keratin and cholesterol. In the skull, these lesions are usually situated either in the intradiploic spaces or subperiosteally. Dermoids and epidermoids account for approximately 4% of all cases of exophthalmos (Pfeiffer & Nicholl, 1948) and are usually sited extraconally. Their characteristic CT appearance has been described (Wende et al, 1977; Blei et al, 1978). Intraconal dermoids are rare but should be considered when the plain radiographic appearances suggest the presence of a slowly expanding benign lesion.

Acknowledgments

We would like to thank Miss C. M. Bannister and Mrs J. Noble for their permission to publish this case

REFERENCES

Blei, L., Chambers, J. T., Liotta, L. A. & Di Chiro, G., 1978. Orbital dermoid diagnosed by computed tomographic scanning *American Journal of Ophthalmology, 85*, 58–61.

Lloyd, G A. S., 1975. *Radiology of the Orbit.* (W. B. Saunders Co., London), pp. 7–29.

Pfeiffer, R. L. & Nicholl, R. J., 1948 Dermoid and epidermoid tumours of the orbit. *Archives of Ophthalmology, 40*, 639–664.

Wende, S., Aulich, A., Nover, A., Lanksch, W., Kazner, E., Steinhoff, H., Meese, W., Lange, S. & Grumme, T., 1977. Computed tomography of orbital lesions. *Neuroradiology, 13*, 123–134.

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Correspondence

(The Editors do not hold themselves responsible for opinions expressed by correspondents)

Metastatic deposits from a previously treated carcinoma of the lung presenting as a renal carcinoma

THE EDITOR—SIR,

We read with interest the paper by Bailey et al (1986) reporting two cases of the above. We wish to describe a similar case, in which surgery could have been avoided if the possibility of metastases from previously treated carcinoma of the lung had been considered.

A 59-year-old woman, with a previously treated squamous-cell carcinoma of the left lower lobe bronchus, presented in November 1985 with a 2-month history of intermittent haematuria and severe right-sided loin pain. Physical examination revealed an ill-defined mass in the right side of the abdomen. Full blood count and biochemistry showed no abnormality. Chest radiography showed fibrosis in the left lower lobe. Intravenous urography demonstrated the possibility of a tumour in the right kidney. At exploration, the upper pole of the right kidney was found to have been replaced by a hard tumour adherent to the peritoneum. The peritoneum was opened but no obvious abnormality was found within the abdomen. After mobilisation of the right kidney it became apparent that there was extensive lymph-node involvement, with tumour around the vascular pedicle of the kidney It proved impossible to remove the full extent of the tumour, so only the kidney was removed. Examination of the kidney showed an ill-defined 5 cm × 4 cm × 3 cm mass in the upper pole, with adherent overlying capsule. Renal tissue elsewhere appeared normal. Microscopy showed poorly differentiated carcinoma with some squamoid features. The appearances were consistent with metastatic carcinoma probably from a bronchial primary. No further treatment was offered and the patient died 2 months later.

Yours, etc.,
RAJNI AMIN,
MICHAEL PAGLIERO

Royal Devon and Exeter Hospital,
Barrack Road,
Exeter

(*Received April 1986*)

REFERENCE

BAILEY, M. J., WILLIAMS, J E. & RIDDLE, P. R., 1986. Metastatic deposits from a previously treated carcinoma of the lung presenting as a renal carcinoma *British Journal of Radiology*, *59*, 333–336.

Green lasers for patient positioning in radiotherapy

THE EDITOR—SIR,

The introduction over the last decade of low power He–Ne lasers has done much to facilitate accurate patient positioning in radiotherapy One problem has been evident, however, in that the degree of subcutaneous diffusion, produced when the characteristic orange-red emission of He–Ne lasers is projected onto skin, causes the inherent resolution of the lines or spots to be lost. A recent development in laser technology, however, has been of a green He–Ne laser operating at 543 nm. Substitution of these green lasers for the conventional orange-red greatly reduces the subcutaneous effect and some additional consequences are also worthy of note, viz.

(a) gentian violet skin marks are more easily visualised;
(b) on account of the much greater sensitivity of the eye to this portion of the spectrum, substantially lower laser output power is required,
(c) many radiographers find the colour much more acceptable for constant viewing.

Although these lasers are at the moment available only from specialist laser manufacturers (such as Melles-Griot (UK) Ltd, Culdrose House, Frederick Street, Aldershot, Hants GU11 1LQ) and so must be coupled by the user to suitable optics (*i e* line or cross generators available from many sources) and also mounted on suitable alignment platforms, the benefits of the change are considerable.

We have recently completed the installation of such a system at Cookridge Hospital.

Yours, etc.
J B. TUOHY

Medical Physics Department,
Regional Radiotherapy Centre,
Cookridge Hospital,
Leeds LS16 6QB

(*Received May 1986*)

Retention of indium 111 by incinerator ash

THE EDITOR—SIR,

While attempting to trace a ^{198}Au grain lost during a radiotherapy implant procedure, the 171 keV and 245 keV cascade γ rays from ^{111}In were detected in samples of hospital incinerator ash. Indium 111 also produces a peak in its γ-ray spectrum at 416 keV, corresponding to the summation of the separate cascade radiations, and detection of remnants of the gold grain was hindered by the similarity between this sum peak energy and the γ-ray energy (412 keV) of ^{198}Au, and by the similarity between the half-lives of ^{111}In and ^{198}Au (67.2 h and 64.2 h, respectively). The clinical use of ^{111}In for *in-vivo* studies with radiolabelled blood cells and radiolabelled antibodies is increasing and, therefore, this retention of ^{111}In by incinerator ash was investigated further

No radioactive waste was incinerated in the following week, during which the incinerator was cleared of ash after each burning. At the end of this period, a sample of ash was retained to determine the background Approximately 3 MBq (80 μCi) of ^{111}In oxine was distributed through glass vials, syringes, tubes and needles, typical of the waste formed from an ^{111}In leucocyte labelling procedure. Two-thirds of the activity was in a 10 ml saline solution contained in a 15 ml plastic conical tube, similar to the redundant supernatant radioactivity formed by centrifuging a leucocyte suspension

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Correspondence

after radiolabelling. This waste was loaded into a "sharps" box, which was then incinerated with the next day's hospital waste. Samples of the ash were collected and their ^{111}In activity was determined with a sodium-iodide well counter.

There was no ^{111}In in the background ash sample and the mean concentration in the active ash samples was found to be 1.1±0.1 MBq m^{-3} (29±3 μCi m^{-3}) It was estimated that the total volume of ash formed from the day's burning was 0.14±0.02 m^3 and, therefore, 5±1% of the ^{111}In had been retained in the incinerator ash.

The Radioactive Substances (Hospitals' Waste) Exemption Order (1983) permits a maximum activity of 1.1 MBq (30 μCi) to be incinerated per day and permits a maximum activity of 0.37 MBq (10 μCi) to be disposed in 0.1 m^3 of ash. Authorisation may be granted to a hospital to increase this daily incineration limit. For the conditions of this study, the maximum activity in 0.1 m^3 of ash would be reached if an incineration limit of 7.4 MBq (200 μCi) per day had been authorised. For a different set of conditions, it may be possible to reach the maximum activity in 0.1 m^3 of ash with a lower authorised incineration limit.

It was also concluded that retention of ^{111}In by incinerator ash and its similar physical characteristics to ^{198}Au must be borne in mind when searching for remnants of the latter in hospital waste.

Yours, etc.,
P. J. MOUNTFORD
J. R. CORFIELD
C. P WELLS

Department of Medical Physics,
Kent and Canterbury Hospital,
Ethelbert Road,
Canterbury,
Kent CT1 3NG

(*Received May 1986*)

REFERENCE

THE RADIOACTIVE SUBSTANCES (HOSPITALS' WASTE) EXEMPTION ORDER, 1963. (Her Majesty's Stationery Office, London), p. 3.

Monitoring of staff wearing lead-rubber aprons

THE EDITOR—SIR,

Diagnostic radiologists at the Whittington Hospital have expressed concern regarding the personal monitoring of staff wearing lead-rubber aprons and the criteria for the designation of classified workers. This letter is a response to their request for clarification and an invitation to comment from other interested parties Where appropriate, I have used direct quotations from references in order to leave no room for ambiguity

On the position of dosemeters, the International Commission on Radiological Protection (ICRP) (1982) states.

> "In special situations where installed shielding or protective clothing such as lead aprons provides significant attenuation of the incident radiation on some parts of the body, more than one dosemeter may be required In particular, the following advice applies in medical radiology, where the use of lead aprons is common. If a single dosemeter is used it should be worn outside of the apron, usually high on the trunk. The recorded result will provide information on the dose equivalent to the skin, eye and unshielded parts of the body (though not necessarily to the hands) but will over-estimate the effective dose equivalent. When the recorded values indicate annual totals approaching dose limits for effective dose equivalent or when realistic estimates for effective dose equivalent are needed as in the optimisation of protection, this overestimation may be unacceptable. Two dosemeters should then be used, one over and one under the protective apron. The interpretation of the combined results will have to depend on the local irradiation conditions and any regulatory requirements."

The current dose limits are given in Schedule 1 (p. 35) of *The Ionising Radiations Regulations 1985* (HMSO, 1985). Part 1 of this schedule relates to dose limits for the wholy body:

> "1. The dose limit for the whole body resulting from exposure to the whole or part of the body, being the sum of the following dose quantities resulting from exposure to ionising radiation, namely the effective dose equivalent from external radiation and the committed effective dose equivalent from that year's intake of radionuclides, shall in any calendar year be—
> (a) for employees aged 18 years or over, 50 mSv
> (b) for trainees aged under 18 years, 15 mSv
> (c) for any other person, 5 mSv."

Part 2 of this schedule refers to dose limits to individual organs only and is to be applied "without prejudice to Part 1". Part 3 is even more specific and relates to dose limits to the lens of the eye. This dose-limit schedule differs from that of Appendix B of the *Code of Practice for the Protection of Persons Against Ionising Radiations Arising from Medical and Dental Use* (HMSO, 1972) in that the whole-body limit is applied to whole- or partial-body irradiation.

The effective dose equivalent is defined as:

$$H_E = \Sigma_T W_T H_T \qquad \text{mSv}$$

where, suffix T is for a tissue or organ, H_T is the tissue or organ dose equivalent and W_T is the tissue or organ weighting factor. Thus, if we are to arrive at an accurate interpretation of the recorded dose equivalent we need to calculate the effective dose equivalent, taking account of the individual organ dose equivalents It may well be possible to arrive at an accurate assessment of the organ dose equivalents from an accidental exposure if there is sufficiently detailed knowledge of the conditions of irradiation. However, it is unlikely that such information will be available in the general case.

What order of magnitude is the overestimate of the effective dose equivalent to a diagnostic radiologist when monitoring with a single dosemeter worn at collar level? Assume that·

(1) there are uniform irradiation conditions,
(2) the lead apron covers the whole of the trunk and $H_{\text{trunk}} \rightarrow 0$,
(3) the subject wears the dosemeter throughout the monitoring period and
(4) the dose recorded by the dosemeter is 1.15 mSv, this being 30% of the whole-body limit for one 28-day month and that this dose is the average tissue dose equivalent for each organ or tissue considered.

Then, for H_T = 1.15 mSv, W_T for: thyroid = 0.03, red bone marrow = 0.06, bone (surfaces) = 0.015, brain = 0.06 and salivary glands = 0.06. The volume of red bone marrow and bone surfaces irradiated is reduced by about a half and so the W_T values have been reduced accordingly. Therefore H_E = 0.259 mSv and the dose recorded is thus 4.5 times larger than the effective equivalent dose. However, the assumption is that the irradiation was uniform over the whole body; if it is not and the recorded dose level was not representative, we introduce further uncertainty which can increase or decrease this factor

Thus, if we accept the advice of the ICRP (1977, 1982), then the following guidelines can be established.

(1) A single over-apron dosemeter should be worn, high on the trunk, on the collar or on the shoulder (Palmer, 1985), such that it cannot be obscured by protective clothing. Additional dosemeters may be positioned, if required, for example under the apron and for extremity monitoring. It is not recommended that the recorded dose from the collar-level dosemeter is used as an assessment of eye dose (Jeans et al, 1985). A more reliable estimate of eye dose may be obtained by using, for example, a strap type extremity dosemeter, containing a thermoluminescent material, fastened to the forehead with a surgical tape such as Micropore.

(2) The annual dose limit to be used for employees wearing a lead apron and a single collar-level dosemeter should be that detailed in Schedule 1, Part 1 of *Statutory Instrument No. 1333* (HMSO, 1985), *i.e.* the whole-body limit

(3) The results of over-apron collar-level monitoring should, in general, be assumed to reflect the effective equivalent dose for the whole body and should, without prejudice to extremity or eye monitoring, form the initial basis of whether to designate an employee as a classified radiation worker. However, it should be noted that, given a set of reasonable assumptions as detailed above, the effective dose equivalent recorded could be 4 5 times too high, with obvious implications for designation criteria.

(4) Hence, if the dose recorded by an employee, from a single collar-level dosemeter, exceeds 30% of any relevant dose limit, an optimisation study in the form of a more extensive monitoring programme to assess the dose equivalents to other exposed radiosensitive organs or tissues, not included in other dose equivalent limits, should be undertaken in order to estimate more accurately the effective equivalent dose and thus confirm or reject the designation of the employee.

I wish to thank Dr C. Doust of the Whittington Hospital Medical Physics Department and Dr M C Thorne, Scientific Secretary to the ICRP, for many helpful comments and suggestions.

Yours, etc.,
J. R. Jones

Medical Physics Department,
The Whittington Hospital,
London N19 5NF
(*Received May 1986*)

REFERENCES

HMSO, 1972 *Code of Practice for the Protection of Persons Against Ionizing Radiations Arising from Medical and Dental Use*.

——1985. *The Ionising Radiations Regulations 1985, Statutory Instrument No. 1333*

ICRP, 1977. Recommendations of the International Commission on Radiological Protection. *Annals of the ICRP, Publication 26*

——1982. General Principles of Monitoring for Radiation Protection of Workers. *Annals of the ICRP, Publication 35*.

Jeans, S. P., Faulkner, K., Love, H. G. & Bardsley, R A., 1985 Routine monitoring of eye dose (reply). *British Journal of Radiology, 58*, 1227–1228.

Palmer, K., 1985. Routine monitoring of eye dose (letter). *British Journal of Radiology, 58*, 1227.

A preliminary study of the possible benefits of using carbon dioxide insufflation during double-contrast barium enema

The Editor—Sir,

We read with interest the article by Grant et al (1986), because we too recently completed a double-blind trial to assess patient discomfort following double-contrast barium enema (DCBE) using CO_2 versus room-air insufflation (Coblentz et al, 1985) Contrary to their findings, we found both a clinically and statistically significant reduction in pain after DCBE when CO_2 was used.

The difference in our result can be explained by the time interval after which the follow-up questionnaire regarding pain was completed. As Grant et al point out, 30 min may be too short a time to wait. Our follow-up questionnaire was presented by telephone 12–24 h after DCBE, and in those patients who experienced pain, the mean time of onset was 2 h.

We believe that immediate patient discomfort is relieved by the antispasmodics which were routinely given both in our study and in that by Grant et al. If the question was asked some time later, then we believe their findings would confirm ours: that 30% of patients will complain of clinically significant pain following DCBE with room-air versus only 10% of patients having CO_2 insufflation ($p < 0.05$).

We administer the CO_2 by a simply constructed and easily used device (Bernier & Coblentz, 1986). The cost of CO_2 is trivial Because of its ease of use and because it reduces pain after DCBE, we routinely use CO_2 in our department.

Yours, etc.,
Craig Coblentz

Department of Radiology,
Faculty of Health Sciences,
McMaster University,
1200 Main Street West,
Hamilton,
Ontario L8N 3Z5
Canada
(*Received April 1986*)

REFERENCES

Bernier, P. & Coblentz, C. L., 1986. A CO_2 delivery system for double-contrast barium enemas. *Radiology, 159*, 264

Coblentz, C. L., Frost, R. A., Molinaro, V. & Stevenson, G W., 1985. Pain after barium enema: effect of CO_2 and air on double-contrast study. *Radiology, 157*, 35–36.

Grant, D. S., Bartram, C I. & Heron, C. W, 1986. A preliminary study of the possible benefits of using carbon dioxide insufflation during double-contrast barium enema. *British Journal of Radiology, 59*, 190–191.

(*Authors' reply*)

The Editor—Sir,

The findings by Coblentz et al supported our initial clinical impression that CO_2 reduced the unpleasant side-effects of double-contrast barium enema examination. The basis for this was the very rapid absorption of CO_2 compared with that of air All available studies indicated that there would be a significant difference within a period of 30 min.

We were rather surprised to find, either clinically or by rough assessment, that there was no obvious difference at that time in the volume of gas remaining in the bowel as shown on the plain radiograph. It is obviously essential to increase the time span of the study, as it now appears that to demonstrate a difference between CO_2 reabsorption and air needs hours rather than minutes.

The assessment of abdominal pain or discomfort is a difficult and tenuous subject. It would be preferable to relate any subjective finding to the volume of gas remaining in the bowel to prove the relationship in any future study.

Yours, etc.,
D. S. GRANT
C. I. BARTRAM

Department of Radiology,
St Mark's Hospital,
City Road,
London EC1V 2PS

(*Received April 1986*)

A comparison of simplified and standard methods for the measurement of glomerular filtration rate and renal tubular function

THE EDITOR—SIR,

Notghi et al (1986) have performed a carefully designed study comparing the precision and accuracy of different methods of measuring renal clearance. However, their conclusion, that the methods involving limited plasma sampling following the intravenous injection of a suitable radioactive tracer are too inaccurate and unreproducible for clinical use, is at variance with much of the current literature on this subject and also with our own experience. The problem would appear to lie with the potentially doubtful accuracy and precision of the "gold standards" used for the measurement of glomerular filtration rate (GFR) and effective renal plasma flow (referred to in the paper as tubular secretion rate), *i.e.* inulin and para-aminohippurate clearance (PAH), respectively. This situation regularly crops up in the assessment of new, and hopefully better, analytical methods where even a perfectly precise and accurate method will not "look good" when correlated against an inaccurate and/or imprecise "gold standard".

Considering the detailed findings of Notghi et al, the best correlation observed by the authors was that for GFR measured using subcutaneously injected ^{125}I-iothalamate against GFR measured by inulin clearance (their Fig. 1). Both measurements were made by the classic "UV/P" method, using urine collections from 1–2 h and 2–3 h after tracer injection. Because the hourly urine collections, V, are common to both the radioactive and stable tracer measurements, if V is inaccurate both methods will give inaccurate results. However, as the two results would be affected proportionately, this will not affect the correlation between them. Therefore, it is possible for a good correlation to be obtained when neither of the methods being compared is necessarily accurate. If the authors had correlated the 1–2 h ^{125}I-iothalamate results against the 2–3 h inulin results or vice versa, then they would obtain a better estimate of the correlation between independent measurements. The fact that they do have two consecutive estimates for both ^{125}I-iothalamate clearance and inulin clearance should allow paired comparisons of the 1–2 h and 2–3 h measurements, which would provide an estimate of the reproducibility of both methods. If the reproducibility of either or both methods is poorer than expected, then this would explain why the scatter about the regression line in their study is greater than that seen in the original reference source for the ^{125}I-iothalamate method (Israelit et al, 1973).

Considering the correlation of GFR, measured by a double plasma sampling method against inulin clearance (their Fig. 2), the standard deviation of the residuals (SDR) would appear to be greater than 30 ml/min. In a recent comparison of other renally filtered tracers, ^{125}I or ^{131}I-diatrizoate, with inulin clearance, Tauxe (1986) obtained an excellent correlation with a SDR of 5.9 ml/min. In this instance, the GFR values obtained using the radioactive tracers were calculated by fitting a two-compartment model to plasma radioiodinated diatrizoate disappearance curves out to 3 or 4 h after injection. Tauxe also showed that when the GFR was predicted from the plasma tracer activity at 3 h only, the SDR when compared with the results obtained using the whole disappearance curve was 7.1 ml/min. Several other workers (Morgan et al, 1977; Constable et al, 1979; Russell et al, 1985) have all compared one- or two-sample methods with analysis of the whole plasma disappearance curve and reported SDR values not greater than 10 ml/min for various filtered tracer, *i.e.* ^{51}Cr-EDTA, ^{99}Tc^{m}-DTPA and ^{169}Yb-DTPA (in the case of ^{99}Tc^{m}-DTPA, correction was made for *in-vivo* plasma binding (Russell et al, 1983)). In our own laboratory, we have measured GFR in 47 patients using a two-compartment model to fit the plasma disappearance curve of intravenously injected ^{51}Cr-EDTA out to 3 h. When we apply the one- or two-sample prediction formulae provided by Morgan, Constable, Russell and their coworkers, the SDR relative to analysis of the whole plasma disappearance curve ranges from 4.2 ml/min to 7.5 ml/min for a single sample at 3 h or two samples in the 1–3 h interval. Therefore, the conclusion of Notghi et al, that the "critical limitation of this approach (*i.e* the limited plasma sample approach) is the cumulative crudity of the mathematical approximations involved" is not supported by the findings of either ourselves or other workers.

Finally, in Fig. 3 of their paper, Notghi et al present the correlation of effective renal plasma flow (ERPF) measured by a two-plasma sample method with the "gold standard" method of PAH clearance where the SDR would appear to be greater than 200 ml/min. This has to be compared to the value of 33.5 ml/min obtained by Tauxe et al (1971) when correlating ERPF calculated from a compartmental analysis of ^{131}I-orthoiodohippurate disappearance curves with PAH clearance. That study and the others listed above have shown that, when one-sample estimates of ERPF are correlated with the ERPF obtained by analysing the whole curve, then the SDR is less than 46 ml/min.

Therefore, despite careful design, it would seem that a substantial part of the scatter seen in the method comparison plots of Notghi et al must result from the poor reproducibility of some of the methods used for estimating GFR, particularly the "gold standard" methods. Unless the authors can prove that the reproducibility of their "gold standard" methods is acceptable, *e.g.* around 5%, we do not feel that they are justified in implying that the limited plasma sample techniques for measuring GFR and ERPF are insufficiently accurate or reproducible.

Yours, etc.,
W. S. WATSON
H. DOBSON
R. HUME

Departments of Nuclear Medicine, Radiology
and Medicine,
Southern General Hospital,
Govan Road,
Glasgow

(*Received March 1986*)

1986, *The British Journal of Radiology*, *59*, 1054–1055

REFERENCES

Constable, A. R., Hussein, M. M., Albrecht, M. P., Thompson, F. D., Philalithis, P. E. & Joekes, A. M., 1979. Single sample estimates of renal clearances. *British Journal of Urology*, *51*, 84–87.

Israelit, A H, Long, D. L., White, M. G. & Hull, A. R., 1973. Measurement of glomerular filtration rate utilizing a single subcutaneous injection of 125I-iothalamate. *Kidney International*, *4*, 346–349.

Morgan, W. D., Birks, J. L., Sivyer, A. & Ghose, R. R., 1977. An efficient technique for the simultaneous estimation of GFR and ERPF, involving a single injection and two blood samples. *International Journal of Nuclear Medicine and Biology*, *4*, 79–83.

Notghi, A., Merrick, M V, Ferrington, C & Anderton, J. L., 1986. A comparison of simplified and standard methods for the measurement of glomerular filtration rate and renal tubular function. *British Journal of Radiology*, *59*, 35–39.

Russell, C. D., Bischoff, P. G., Kontzen, F. N., Rowell, K. L., Yester, M. V., Lloyd, L. K., Tauxe, W. N. & Dubovsky, E. V., 1985. Measurement of glomerular filtration rate: single injection plasma clearance method without urine collection. *Journal of Nuclear Medicine*, *26*, 1243–1247.

Russell, C. D., Bischoff, P. G., Rowell, K. L., Kontzen, F., Lloyd, L. K, Tauxe, W. N. & Dubovsky, E. V., 1983. Quality control of Tc-99m DTPA for measurement of glomerular filtration: concise communication. *Journal of Nuclear Medicine*, *24*, 722–727.

Tauxe, W. N., 1986. Determination of glomerular filtration rate by single-plasma sampling technique following injection of radioiodinated diatrizoate. *Journal of Nuclear Medicine*, *27*, 45–50.

Tauxe, W. N., Maher, F. T. & Taylor, W. F., 1971. Effective renal plasma flow: estimation from theoretical volumes of distribution of intravenously injected 131I orthoiodohippurate. *Mayo Clinic Proceedings*, *46*, 524–531

Author's reply

The Editor—Sir,

We read with interest the letter of Dr Watson and his colleagues. We quite agree with their comment that there is no "gold standard" for measurement of glomerular filtration rate (GFR) and have even greater doubt about the validity of PAH clearance measurement. We, however, considered comparison with inulin and PAH justified on account of the historical dependence of renal function measurement on these methods, for which, so far, there is no universally accepted replacement. The problems with most new methods arise when they are applied for clinical purposes outside the strictly controlled laboratory conditions in which they were introduced. It was for this reason that we chose to use clinically convenient sampling periods. As we stated, multiple sampling techniques over an extended period, which permit the time–clearance curve to be accurately delineated, are well validated. The question was whether the simplifications which have been proposed are sufficiently reliable to be clinically useful.

When we compared iothalamate with inulin clearance, we chose to compare the same hourly periods to avoid introducing the additional factor of inaccuracy in urine collection during consecutive collections. When reproducibility of these methods is tested, in addition to methodology, changes in human renal function with rest, emotion, food, posture, disease and diurnal variation make consecutive comparisons less meaningful, even during a comparatively short period of a few hours. For this reason we chose to compare the changes detected by two methods rather than looking into reproducibility of data over two consecutive measurements by the same method.

As no method of estimation of GFR and renal blood flow has yet emerged which is clearly superior and easy to perform, creatinine clearance will probably continue to be widely used as a convenient method for follow-up of renal function in clinical practice.

Yours, etc.,
A. Notghi
M. V. Merrick
C. Ferrington
J. L. Anderton

Medical Radioisotope Department,
Western General Hospital,
Edinburgh EH4 2XU

(*Received March 1986*)

A comparison of simplified and standard methods for the measurement of GFR and renal tubular function

The Editor—Sir,

Notghi et al (1986) reported a comparison of the classical measurements of glomerular filtration rate (GFR) and effective renal plasma flow (ERPF) using a constant infusion of inulin and para-aminohippurate (PAH) with plasma and urine collection, with a simplified procedure for the measurement of GFR and ERPF employing intravenous administration of two radiopharmaceuticals and the taking of two blood samples which was developed in our department (Smart et al, 1981). The results of Notghi et al did not appear to support the use of the simplified procedure as a replacement for the classical clearance measurements of inulin and PAH.

Several comments on the study of Notghi et al need to be made. Our reported method for GFR determination employed ^{51}Cr-EDTA as the tracer, while Notghi employed ^{99}Tc^{m}-DTPA. Renal clearance measurements using ^{51}Cr-EDTA compare extremely well with simultaneously performed inulin clearances (Garnet et al, 1967; Lavender et al, 1969). Furthermore, the renal clearance rates have been shown to be accurately determined by monitoring the plasma clearance of intravenously administered ^{51}Cr-EDTA (Bröchner-Mortensen et al, 1969, Vögeli et al, 1971). Hilson et al (1976) proposed ^{99}Tc^{m}-DTPA as an alternative radiopharmaceutical for the measurement of GFR. However, later authors have reported significant problems when using ^{99}Tc^{m}-DTPA similar to those experienced by Notghi et al. Carlsen et al (1980) reported markedly different results using preparations of DTPA from four different manufacturers; Russell et al (1983) reported significant protein-binding of the ^{99}Tc^{m}-DTPA; and our own, unpublished results indicate variations in ^{99}Tc^{m}-DTPA clearance with pertechnetate from different manufacturers. Although ^{99}Tc^{m}-DTPA is used in our institution for renal imaging and for the determination of relative renal function, we continue to use ^{51}Cr-EDTA for the measurement of GFR because of the variable *in-vivo* behaviour of ^{99}Tc^{m}-DTPA. Furthermore, the "gold standard" used by Notghi et al for

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Correspondence

GFR, the renal clearance of inulin, involves the chemical determination of inulin. The authors noted that the reproducibility of their inulin measurements was poor, which undoubtedly accounted for part of the variability in their results

Our method for the determination of GFR and ERPF from only two samples involved calculating a clearance rate, F, assuming a single exponential clearance, and then applying an empirically derived correction factor to account for the true multiexponential nature of the clearance curves. Our regression equations for GFR and FRPF were:

$$\mathrm{GFR} = 1.0+0.9\,F$$
$$\mathrm{ERPF} = 5.0+0.875\,F-0.469\times10^{-3}\,F^2+0.127\times10^{-6}\,F^3$$

Notghi et al have calculated the clearance rate but do not appear to have corrected their values to account for the overestimation of the clearance rate by the monoexponential assumption. They, in fact, comment that they found higher values for the ^{131}I-orthoiodohippurate (OIH) clearance than for the PAH clearance This is to be expected if the two-sample method is used without applying the above corrections

We maintain that if ^{51}Cr-EDTA is employed for the measurement of GFR and if ^{125}I-OIH, with minimal free ^{125}I, is employed for the measurement of ERPF, together with the corrections to the clearance rates, accurate and reproducible measurements will be obtained

Yours, etc.,
R C. Smart
N. R Lyons

Nuclear Medicine Department,
The St George Hospital,
Belgrave Street,
Kogarah,
2217 New South Wales, Australia
(*Received May 1986*)

REFERENCES

Bröchner-Mortensen, J., Giese, J. & Rossing, N., 1969. Renal inulin clearance versus total plasma clearance of ^{51}Cr-EDTA. *Scandinavian Journal of Clinical and Laboratory Investigation*, *23*, 301–305.

Carlsen, J. E., Møller, M. L., Lund, J O. & Trap-Jensen, J., 1980. Comparison of four commercial Tc-99m (Sn) DTPA preparations used for measurement of glomerular filtration rate: concise communication. *Journal of Nuclear Medicine*, *21*, 126–129.

Garnet, E. S., Parsons, V. & Veall, N., 1967. Measurement of glomerular filtration rate in man using a ^{51}Cr/edetic-acid complex. *Lancet*, *i*, 818–819.

Hilson, A. J. W, Mistry, R. D & Maisey, M. N., 1976. ^{99}Tc^{m}-DTPA for the measurement of glomerular filtration rate *British Journal of Radiology*, *49*, 794–796.

Lavender, S., Hilton, P. J & Jones, N. F, 1969. The measurement of glomerular filtration rate in renal disease. *Lancet*, *ii*, 1216–1218.

Notghi, A., Merrick, M. B., Ferrington, C. & Anderton, J., 1986. A comparison of simplified and standard methods for the measurement of glomerular filtration rate and renal tubular function. *British Journal of Radiology*, *59*, 35–39.

Russell, C. D, Bischoff, P. G, Rowell, K. L., Kontzen, F., Lloyd, L. K., Tauxe, W. N. & Dubovsky, E. V., 1983. Quality control of Tc-99m DTPA for measurement of glomerular filtration: concise communication. *Journal of Nuclear Medicine*, *24*, 722–727.

Smart, R., Trew, P, Burke, J. & Lyons, N., 1981. Simplified estimation of glomerular filtration rate and effective renal plasma flow. *European Journal of Nuclear Medicine*, *6*, 249–253.

Vögeli, R., Riedwyl, N., Donath, A. & Oetliker, O., 1971. Comparison of glomerular filtration rate and effective renal plasma flow determinations obtained by a single-injection technique and by means of a standard clearance technique in children *Acta Paediatrica Scandinavica*, *60*, 528–532.

Acute angioneurotic oedema following a barium meal

The Editor—Sir,

We would like to report what is almost certainly an uncommon reaction to Buscopan (hyoscine-N-butylbromide, Boehringer Ingelheim) which we use as a routine hypotonic agent for double-contrast barium meals

Case Report

A 70-year-old man with a long standing sideroblastic anaemia was admitted with a chest infection and upper abdominal discomfort. He was treated with physiotherapy and oral ampicillin and several days later, when he had recovered, a barium meal was performed. One hour after the barium meal, during which 20 mg Buscopan was administered intravenously, he developed large (up to 6 cm × 6 cm) patches of urticaria and angioneurotic oedema on his limbs and face. He had no respiratory difficulty. His antibiotic was stopped and he was treated with chlorpheniramine (Pinton, Allen & Hanburys Ltd) and prednisolone following which his lesions disappeared over 3 days No chronic sequelae developed. For a subsequent infection he was treated with azlocillin (a penicillin derivative) with no untoward effect. He had no history of previous allergic reactions

Buscopan is used as the routine hypotonic agent for double-contrast barium studies in many centres, the usual dose being 20–30 mg intravenously (Hunt & Anderson, 1976). It is an anticholinergic agent acting on parasympathetic ganglia and the common unwanted effects include loss of accommodation, dryness of the mouth, tachycardia and urinary retention (Kreel, 1975; Hunt & Anderson, 1976). Sensitivity to Buscopan is very rare and we have been able to find only one case recorded in the literature. Robinson and Teeling (1982) describe a patient who developed angioneurotic oedema 1 week after starting an oral course of Buscopan They felt that although the clinical picture of their patient would suggest an immediate-type hypersensitivity, the timing was more in keeping with an Arthus reaction. The reaction of our patient is typical of an immediate-type hypersensitivity, by both its timing and nature. It is likely that there was an interaction by another environmental agent related to the recent chest infection. The possibility of reaction to barium is remote since insoluble barium sulphate is not absorbed, although Gelfand et al (1985) indicate that additives to the barium suspension may be responsible for the very rare reactions that are seen They also reported probable reactions to the other commonly used hypotonic agent, glucagon.

In our patient the lack of reaction to another penicillin makes it difficult to implicate ampicillin. The patient was unwilling to be tested intradermally for reaction to Buscopan for fear of a severe reaction.

We believe that, although this possible reaction to Buscopan is rare, it should be recorded and made known.

Yours, etc.,
A. M. K. THOMAS,
*A. M. KUBIE
*R. P. BRITT

Departments of Radiology and *Haematology,
Hillingdon Hospital,
Uxbridge,
Middlesex UB8 3NN

(*Received April 1986 and in revised form May 1986*)

REFERENCES

GELFAND, D. W., SOWERS, J. C., DEPONTE, K. A., SUMNER, T. E. & OTT, D. J., 1985. Anaphylactic and allergic reactions during double-contrast studies: is glucagon or barium suspension the allergen? *American Journal of Roentgenology, 144*, 405–406.

HUNT, J. H. & ANDERSON, I. F., 1976. Double contrast upper gastrointestinal studies. *Clinical Radiology, 27*, 87–97.

KREEL, L., 1975. Pharmaco-radiology in barium examinations with special reference to glucagon *British Journal of Radiology, 48*, 691–703.

ROBINSON, A C. R. & TEELING, M., 1982. Angioneurotic oedema and urticaria induced by hyoscine butylbromide. *Postgraduate Medical Journal, 58*, 316.

October 1986

Monitoring of persons not designated as classified workers

(Memorandum from the BIR Radiation Protection Committee)

Both the current (1972) *Code of Practice for the Protection of Persons Against Ionising Radiations Arising from Medical and Dental Use* and the *Ionising Radiations Regulations 1985* require that persons occupationally exposed to ionising radiations shall be designated as classified workers unless "it is most unlikely that they will exceed three-tenths of any maximum permissible dose" (1972 Code) or three-tenths of the relevant dose limit (*Ionising Radiations Regulations*)

In the past, the distinction between the two categories of occupationally exposed persons tended to be indistinct, as attempts to place workers in the undesignated category required a value judgment to be made in each case As a result, before the Euratom Directive of 1974 it was customary in many cases for hospitals and employing authorities to take the line of least resistance and treat all occupationally exposed persons as though they were designated. The gradual realisation of the implications of the *Ionising Radiations Regulations*, with their requirement for regular medical examinations of classified workers and for the maintenance of radiation records by a laboratory approved for the purpose by the British Calibration Service, has led to a re-examination of the situation, with the result that the application of the three-tenths rule has meant that the great majority of workers in the National Health Service and in other hospitals and in medical laboratories who are occupationally exposed to radiation and who were previously designated as classified workers are already, or shortly will be, de-designated.

Concern has been expressed that this situation might lead employers to stop the monitoring of these workers, particularly at a time when health authorities are increasingly having to decide between undesirable alternatives in restricting funding. Without definitive statutory guidance by the new *Ionising Radiations Regulations* on a need for continued monitoring and record-keeping, it is clear that resource will *not* necessarily be made available for this at individual district health authority level

A central facility for monitoring of occupationally exposed persons dates from the 1940s, when the National Physical Laboratory provided a radiation monitoring film service, later taken over by the Radiological Protection Service (RPS) at Sutton Due to the inherent level of fog which characterises the processing of photographic films, in the early days of the monitoring film service operated by the RPS, the threshold of measurement was originally set at 50 mrem (500 μSv), being changed to 20 mrem (200 μSv) in November 1959 During this period, due to dramatic improvement in standards of radiation protection, the recorded doses for occupational exposure to radiation fell rapidly and this reduction continued into the early and middle 1960s The adoption of thermoluminescent dosemeter monitoring by some departments has resulted in elimination of this threshold and, thus, for the first time, the presentation of an accurate picture of occupational exposure patterns among medical workers.

A problem therefore arises in the case of persons monitored with films that, before November 1959, there is a spurious threshold dose of up to 1300 mrem (13 mSv) recorded annually as occupational exposure for persons monitored on a fortnightly basis, and since November 1959 of up to 520 mrem (5.2 mSv). The situation is further complicated by the fact that, in addition to the RPS service, now provided by the National Radiological Protection Board (NRPB), there are about 27 radiation monitoring services operating in the medical sector in the United Kingdom and these will have had, from time to time, many different conventions of recording and reporting doses.

Despite the limitation of the quality of the data, the BIR feels that it would be unwise to dispose of any recorded data relevant to occupational exposure, whether for persons now designated as classified workers or as other persons. Only by keeping such records will it be possible to carry out retrospective studies of the effects of occupational exposure upon health dating from times when radiological protection standards were less stringent than today. With regard to records of present and future doses arising from the monitoring of non-designated persons, it must be made clear that in the context of the *Ionising Radiations Regulations 1985* the term "records" has a specific legal significance far in excess of what we would visualise as being required to furnish the information necessary to establish annual cumulative dose records of non-designated persons. Since, for these persons, it is necessary to determine an action level, below any dose equivalent limits, at which an investigation is initiated, one could specify that records are kept of doses at this level and above. It follows that if this level is, for example, 500 μSv (50 mrem) and the person concerned is subject to monthly monitoring, then they cannot exceed an annual 6 mSv (600 mrem) without being investigated on at least one occasion, and could then be included in a simple record-keeping system. One could say with certainty that the workers for whom records were not maintained *never* exceeded this particular annual cumulative dose. If required, the investigation level could be set lower, bringing into force the mechanism for generating a new record for the person concerned. It is, however, important that any initiative to set up this simple system is not diminished through attempts to introduce complex arrangements for record-keeping. We would hope that resource would be made available by health authorities to provide such a simple system as can be managed on stand-alone microcomputers, which exist in most departments. We therefore make the following recommendations

(1) No existing radiation dose records or raw data which will allow greater refinement of radiation dose estimates of persons occupationally exposed to radiation in the past should be destroyed.

(2) Although no longer required by statute, monitoring procedures should be maintained for undesignated persons who are, in the generally understood meaning, "radiation workers". This would include all staff in imaging and radiotherapy departments currently monitored.

(3) Consideration should be given to the feasibility of carrying out dose/mortality studies on radiographers (and possibly hospital physicists) employed before 1960, as the occupational radiation exposures were higher in earlier days than more recently and any adverse effects are more likely to be discovered in this group than in current employees.

(4) Health authorities should be directed to provide resource for the maintenance of simple records of radiation exposure of all workers at present monitored.

American Journal of Physiologic Imaging

This is a new quarterly journal publishing original work regarding the efficacy of imaging modalities, and review articles. The publishers intend to cross traditional disciplinary lines and to provide an academic forum for physicians involved in both direct and indirect patient care, and research scientists. It is aimed at those interested in the study of physiology and pathophysiology using imaging techniques.

The first issue of the journal runs to 58 pages and carries six research papers, for example on "Hepatobiliary imaging: the diagnostic use of intravenous morphine in fasting patients" and "The preliminary evaluation of Mn DTPA as a potential contrast agent for nuclear magnetic resonance imaging", as well as two "current concept" review articles. The journal is well designed and carries high-quality reproductions. *ISSN 0885-8276, $95 in US, $107 outside US (Alan R Liss, New York).*

Press releases

New duplex scanner permits real-time measurement of blood flow

In response to the growing demand for low-cost, dedicated peripheral vascular duplex imaging, Sonicaid's development department has evolved imaging electronics to a high level of performance, integrating Doppler with high-resolution imaging. First production units of the new equipment, Vasoview, are scheduled for demonstrations in the summer of this year in the USA and Western Europe. The scanner presentation uses 256 grey scales, which greatly improves the resolution between different tissue types, permitting characterisation of plaque morphology. Doctors and radiologists will value the easier interpretation resulting from an image focused over the entire field-of-view, providing uniform high-resolution. The investigation of carotid arteries, and the arteries and veins in the upper and lower limbs, should be facilitated by this compact diagnostic system, which also offers an integral hand-held CW Doppler.

For the duplex Doppler system, Sonicaid has decided on the wide gate approach, since this has the extended frequency response to permit detection of high-frequency shifts in tight stenoses, and is necessary for insonating the entire vessel to obtain continuous measurement of blood flow and velocity. The company intends soon to introduce pulsed Doppler as an option for users requiring volume element measurement.

Measurement of blood flow in real-time, as provided by Vasoview, is an innovation made possible through Sonicaid's own spectrum analyser and use of a high-speed 32-bit microprocessor. The mean velocity of the blood is calculated in real-time and multiplied by the vessel cross-sectional area. Careful application of the latest technology has created a sophisticated instrument which is, none the less, simple to operate. Further details are available from Sonicaid Limited, Quarry Lane, Chichester, West Sussex PO19 2LP.

Ultrasound image quality improvements for radiology applications

A new revision for Hewlett-Packard Company's phased-array ultrasound imaging system (Model 77020) is designed to improve image quality, particularly for radiology, obstetrics/gynaecology, abdominal, neonatal and shared clinical services applications. The manufacturers say that clinical trials showed as much as 30% improvement in image quality as a result of this revision.

The improvements are the result of several advanced technological enhancements. A digital image-processing technique has been incorporated to produce superior tissue differentiation. Because the signal-to-noise ratio is improved, the image has greater detail and clarity. In addition, an operator now can change the ultrasound beam formation by varying the transducer's transmit focus, this permits the operator to optimise resolution at specific regions of clinical interest.

For further information please contact Louise Blakeborough, Medical Products Group, Hewlett-Packard Limited, Harman House, No 1 George Street, Uxbridge, Middlesex UB8 1YH (Tel. 0895-72020).

Library news

The BIR Library is open weekdays 9 a.m.–5 p.m. (7 p.m. on Thursdays)

The Librarian, Mrs Gunnel Ingham, is in attendance Tuesdays 11 a.m.–5 p.m., and Thursdays 11 a.m.–7 p.m., and Mrs Angela Lansdown, daily 9 a.m.–5 p.m. (Tel. 01-580 4085).

The journal stock includes more than 100 titles. Though journals may not be taken out of the library, there is a photocopy service, also available by post. A list of current journals is available on request and is also published in the March and September issues of the Bulletin.

Most books (excepting the historical collection) are available on loan.

Recent additions to the Library

National Health Service Training Authority: Better management, better health. (Management education and development review.) 1986

Rossetti, G.: Double-contrast radiology of the oesophagus. 1985

Sanders, R. C. & James, A. E. (Eds): The principle and practice of ultrasonography in obstetrics and gynecology. 3rd edit. 1985

Serjeant, G.R.: Sickle cell disease. 1985

Spindola-Franco, H. & Fish, B. G.: Radiology of the heart. 1985

BIR calendar events

Unless otherwise indicated, enquiries about the following events should be addressed to the Assistant Secretary: Programme, British Institute of Radiology, 36 Portland Place, London W1N 3DG (Tel. 01-580 4085).

The meetings are at 36 Portland Place unless otherwise stated. Attendance is open to non-members.

Accelerated Fractionation and Hyperfractionation: experimental and clinical

November 14, 1986 at 11 a.m.
Organised by the Radiobiology Subcommittee. To conclude with the Silvanus Thompson Memorial Lecture: "Cancer—the failure of treatment" by Dr R. H. Thomlinson.

Diagnostic and Therapeutic Uses of Radioisotopes in Oncology

November 26, 1986 at 10.30 a.m.
All day meeting organised by Nuclear Medicine Subcommittee.
Chairmen: Professor R. J. Berry and Dr R. T. D. Oliver. Speakers: Dr I. Fogelman, Dr A. Laing, Dr D. M. Ackery, Dr N. W. Garvie, Dr M. Granowska, Dr A. Epenetos, Dr S. Clarke, Dr P. N. Plowman and Dr V. R. McCready.

Practical Aspects of Magnetic Resonance Imaging

January 14, 1987
Middlesex Hospital Medical School, London
Joint BIR/RCR meeting.

Uroradiology Update

January 15, 1987 at 5.30 p.m.
Chairman: Dr D. Rickards. Speakers: Dr D. Rickards, Dr J. Pemberton, Dr C. E. L. Freer, Mr G. Watson, Dr R. Johnson, Dr W. Lees, Professor D. J. Allison.
Joint BIR/RCR/RSM meeting.

Radionuclide Investigations of the Lung

February 11, 1987
Joint IPSM/BIR (Nuclear Medicine Subcommittee) all day meeting organised by IPSM.

All day non-topic proffered papers meeting

February 13, 1987
Joint ARR/BIR (Radiobiology Subcommittee) meeting organised by the Association for Radiation Research.

Picture Archiving and Communications Systems

February 25, 1987
Venue to be announced
Chairman: Professor I. Isherwood. Topics will include image display, image transmission and image storage. All day meeting organised by Industry Committee.

Annual General Meeting

May 14, 1987 at 4.30 p.m.

Imaging in Radiotherapy

May 15, 1987
Chairmen: Dr D. Thwaites and another to be announced.
Joint IPSM/BIR all day meeting organised by IPSM.

Advance Notice

British Institute of Radiology 45th Annual Congress, incorporating the joint BIR/RCR/RSM (Section of Radiology) spring meeting

RADIOLOGY '87

University of Southampton
April 1–3, 1987

The Congress will cover all aspects of radiology—X-ray diagnosis, radiotherapy, radiation oncology, nuclear medicine, ultrasound, NMR, radiological physics, radiobiology, radiation protection and related disciplines and is expected to include:

The BIR Mackenzie Davidson Memorial Lecture, by Professor M. J. Peckham, "The clinical biology of testicular germ cell tumours"
The BIR Mayneord Lecture (sponsored by 3M UK plc), by Dr Frances Fry, "Chernobyl reactor accident—the impact on the United Kingdom"
The RCR George Simon Lecture, by Dr J. C. Batten
The BIR Presidential Address, by Professor R. J. Berry, "The Institute at 90—a time for reappraisal?"

The BIR Annual Dinner will be held at the Polygon Hotel, Southampton, on April 2.

Proffered papers and posters are invited. Please apply to BIR for form. Absolute closing date for receipt of completed proffered paper forms is November 30, 1986.

For further information please apply to the Assistant Secretary: Programme, The British Institute of Radiology, 36 Portland Place, London W1N 3DG (Tel. 01-580-4085).

Dysphagia and Disorders of Swallowing

May 20, 1987
Royal Society of Medicine, London
Joint RSM/RCR/BIR all day meeting to be organised by the RSM.

Conversazione

May 20, 1987
Royal Naval College, Greenwich

Meetings and courses

As a service to our readers, the title, date and place of meetings and contact address will be inserted free of charge: any additional information will be charged at £1.75 per printed line, per insertion. Please contact the Managing Editor.

Public Perception of Radiation
October 14, 1986
City Conference Centre, London
Further details: Programme Committee Secretary, Professor J. H. Martin, Department of Medical Biophysics, Building 15, Park Wynd, University of Dundee, Dundee DD1 4HN.

Radiology Update
November 7–8, 1986
Cape Town, South Africa
Further details: Prof. B. J. Cremin or Mrs Elliot, Postgraduate Medical Centre, UCT Medical School, Observatory 7925, Cape Town, South Africa (Tel. 021-47 1250).

6th International Conference on Otorhinolaryngology: latest advances in imaging
November 20–22, 1986
Barcelona, Spain
Further details: Dr C. R. Guirado, The Institute of Radiology, Muntaner, 239, Entlo A, 08021 Barcelona, Spain (Tel. 010 343-200 3200).

The Biological Effects of Ionising Radiation
November 24–25, 1986
Royal Postgraduate Medical School, Hammersmith Hospital, London
Further details: Dr Gari Donn, 8 Buckingham Road, Brighton, East Sussex BN1 3RA (Tel. 0273-202516).

Age-Related Factors in Radionuclide Metabolism and Dosimetry
November 26–28, 1986
Angers
Further details: Dr G. B. Gerber, Commission of the European Communities, DG XII/FI, Rue de la Loi 200, B-1049 Brussels, Belgium (Tel. 02-235 4041).

Symposium on Isotope Imaging in Clinical Practice
November 28, 1986
Glasgow
Further details: Dr A. D. Beattie, Royal College of Physicians and Surgeons of Glasgow, 234/242 St Vincent Street, Glasgow G2 5RJ.

The British Medical Ultrasound Society 18th Annual Scientific Meeting
December 16–18, 1986
University of Warwick, Coventry
Further details: Mrs L. Blench, General Secretary, BMUS, 36 Portland Place, London W1N 3DG (Tel. 01-636 3714).

Meeting of the International Working Party for the Diagnosis and Treatment of Carcinoma of the Cervix in Developing Areas
January 23–29, 1987
Calcutta
Further details: Dr Margaret Snelling, 7 Elm Place, London SW7 3QH.

Advanced Course in Diagnostic Imaging
February 8–13, 1987
Singapore
Further details: Professor Lenny Tan, Academy of Medicine, PO Box 694, Tiong Bahru Post Office, Singapore 9116, Republic of Singapore.

Computed Body Tomography 1987: the cutting edge
March 5–8, 1987
Peabody-Orlando Hotel, Florida, USA
Further details: Program Co-ordinator, Office of Continuing Education, Turner 22, 720 Rutland Avenue, Baltimore, Maryland 21205, USA (Tel. 301-955 5880).

British Nuclear Medicine Society Annual Congress
April 12–15, 1987
Imperial College, London
Further details: Mrs A. Taylor, BNMS Conference Secretary, 22 Leinster Avenue, East Sheen, London SW14 7JP.

The Finzi Lecture
April 15, 1987
Royal Society of Medicine, London
"The solitary pulmonary nodule" by Dr S. Segalmann.
Further details: RSM.

3rd European Symposium on Radiopharmacy and Radiopharmaceuticals
May 1–4, 1987
Elsinore, Denmark
Further details: Elisabeth Nørbygaard, The Isotope Pharmacy, 378 Frederikssundsvej, DK-2700 Brønshøj, Denmark.

Conference on Health Effects of Low Dose Ionising Radiation—Recent Advances and Their Implications
May 11–14, 1987
Royal Institute of British Architects, London
Further details: The Secretariat, British Nuclear Energy Society at the Institution of Civil Engineers, 1–7 Great George Street, London SW1P 3AA (Tel. 01-630 0726).

17th Annual Fleischner Society Symposium on Chest Disease
May 21–23, 1987
San Francisco, USA
Further details: Nomi Feldman, 3770 Tansy, San Diego, CA 92121, USA (Tel. 619-453 6222).

VI Congress of the European Association of Radiology (ECR '87)
May 31–June 6, 1987
Lisbon, Portugal
Further details: Secretariat ECR '87, SPRMN, Av. Elias Garcia, 123-7º DTo, 1000 Lisboa, Portugal, (Tel: 77-05 30, Telex 62074 SPRMN P).

College of Radiographers' Annual Conference
July 1–3, 1987
Scarborough
Further details: Miss C. Aldridge, College of Radiographers, 14 Upper Wimpole Street, London W1M 8BN (Tel. 01-935 5726, ext. 206).

HPA Annual General Meeting and IPSM Scientific Meeting
September 15–19, 1987
Liverpool
Further details: IPSM, 47 Belgrave Square, London SW1X 8QX (Tel. 01-235 6111).

5th Asian-Oceanian Congress of Radiology
September 21–25, 1987
Seoul, Korea
Further details: Man Chung Han, M.D., Secretary General, 5th Asian-Oceanian Congress of Radiology, c/o Department of Diagnostic Radiology, Seoul National University Hospital, 28 Yunkun-dong, Chongro-ku, K.P.O. Box 1880, Seoul 110, Korea.

Automation Means in Preventive Medicine '87
September 28–October 2, 1987
Pestany, Czechoslovakia
Further details: The Industry and Technology Division, United Nations Economic Commission for Europe, Palais des Nations, CH-1211 Geneva 10, Switzerland.

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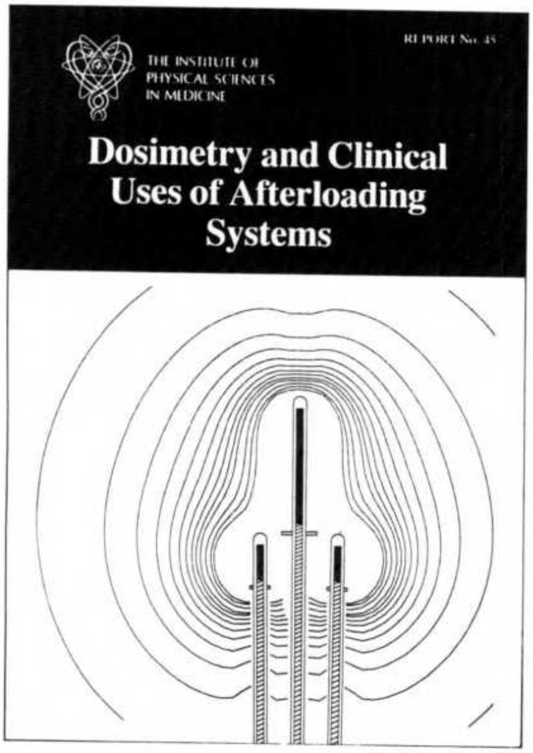

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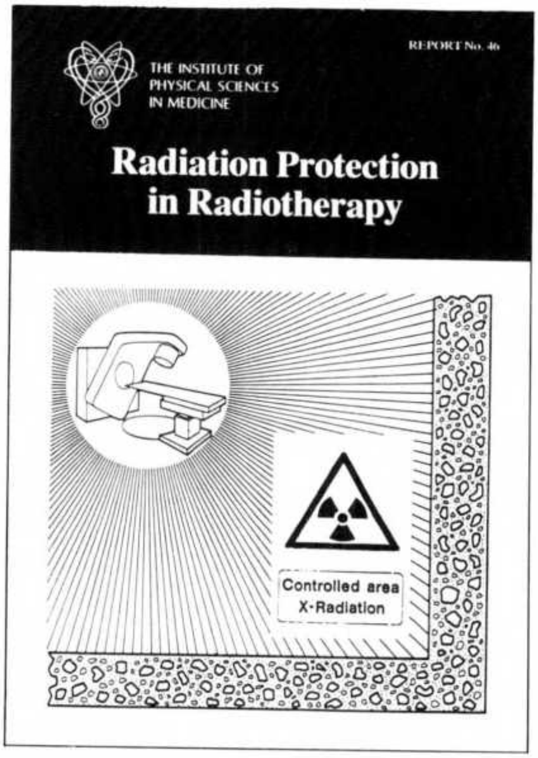

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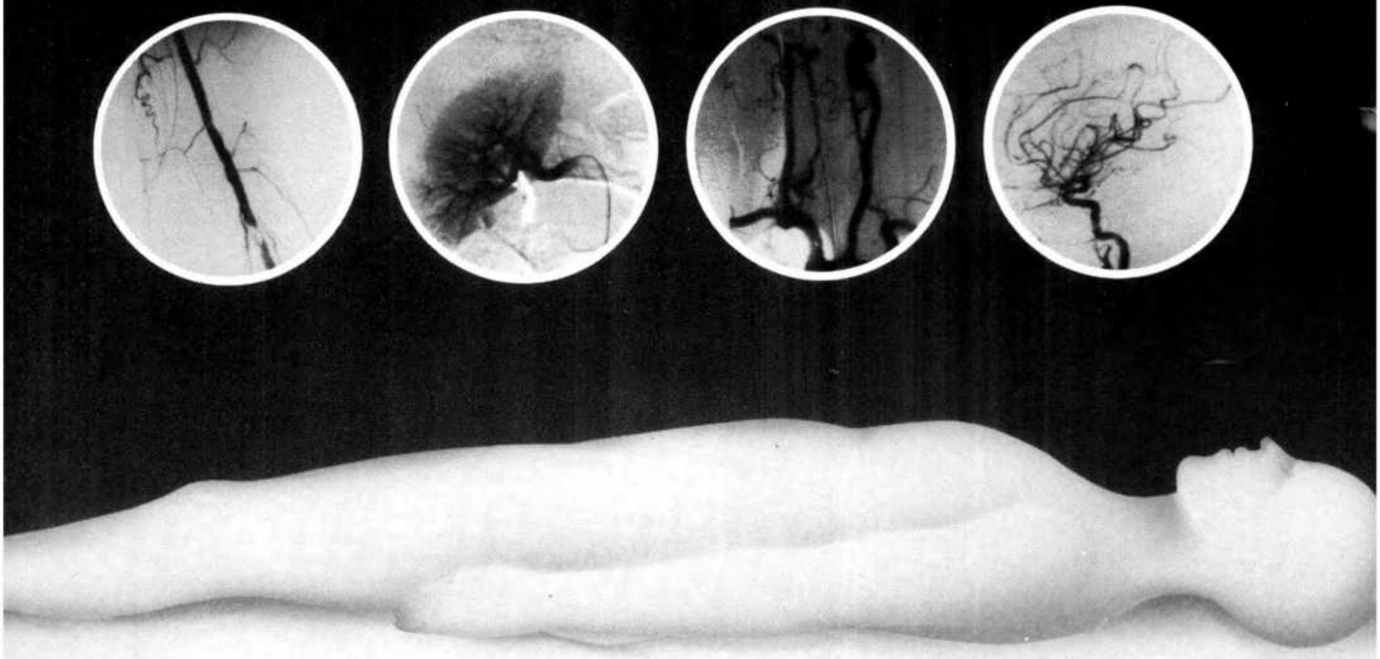

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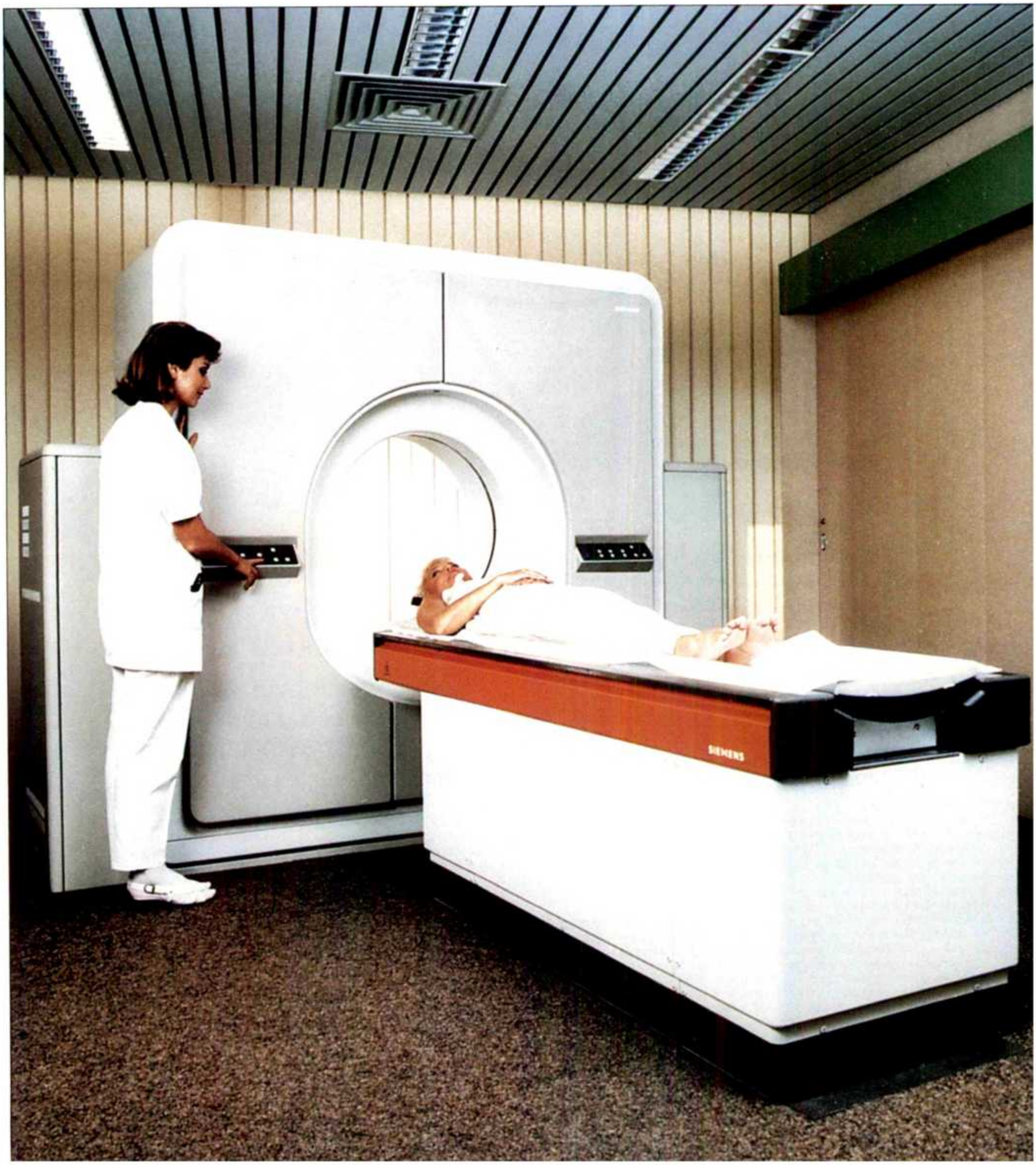

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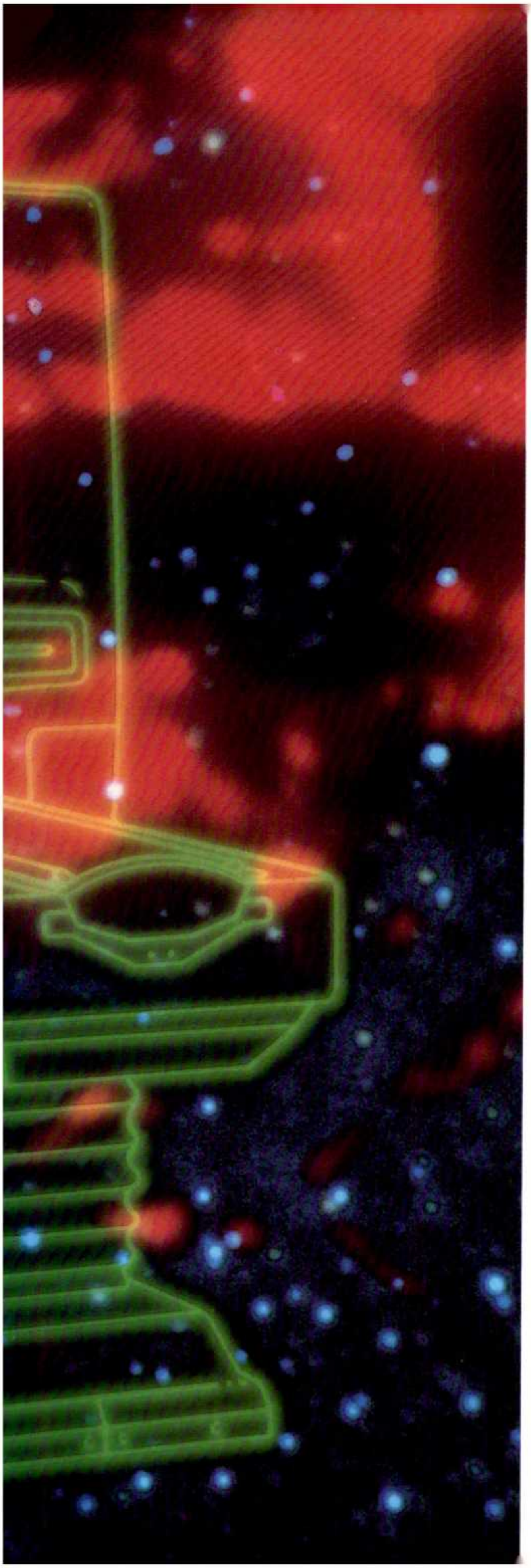

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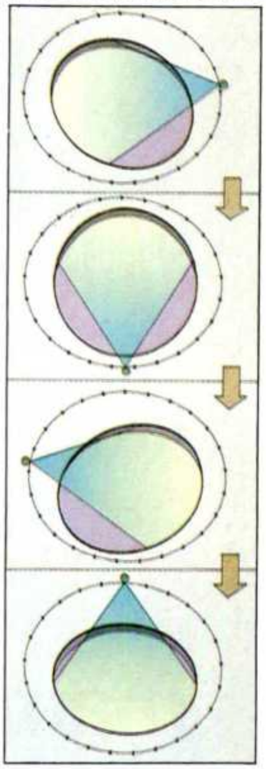

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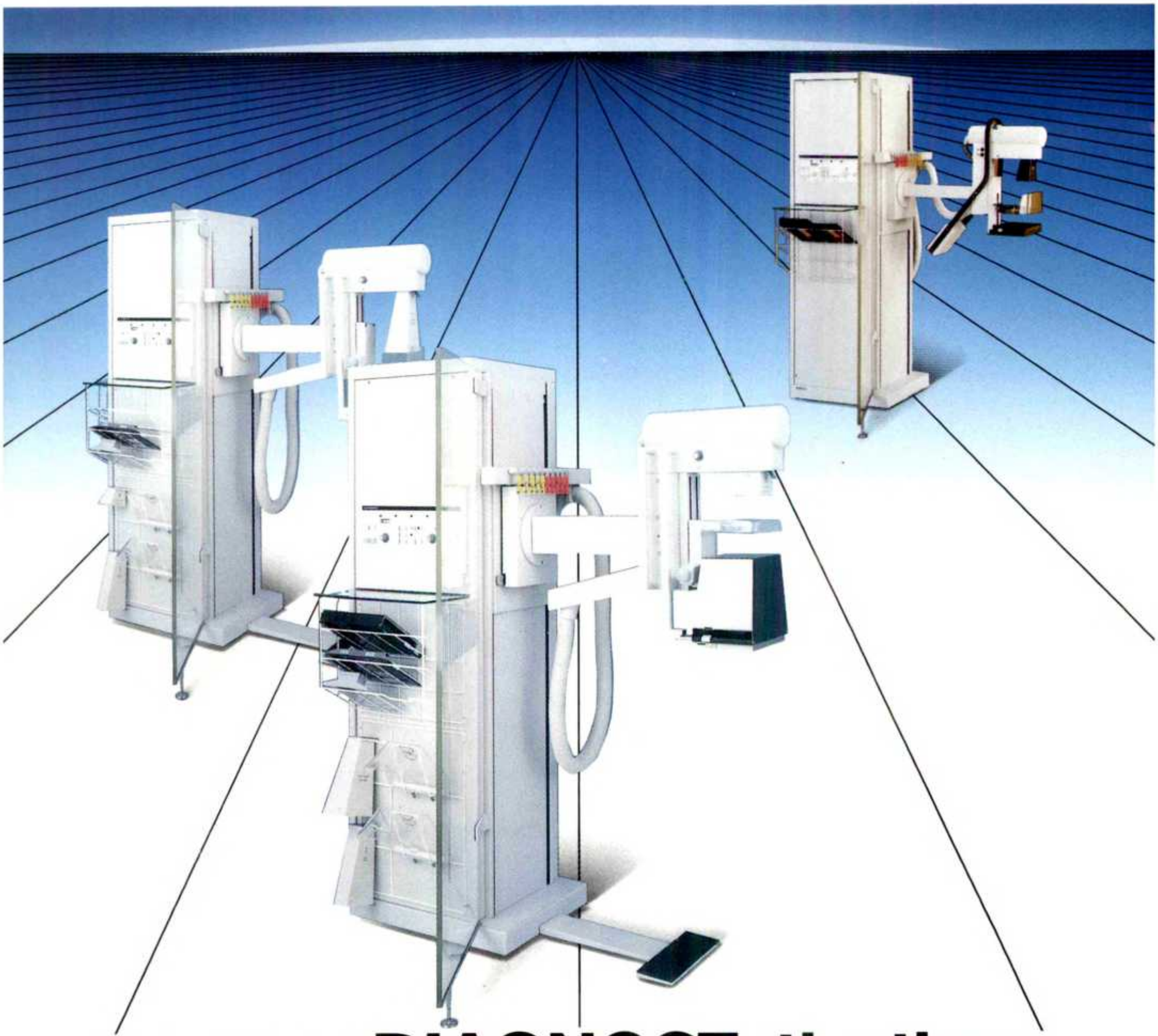

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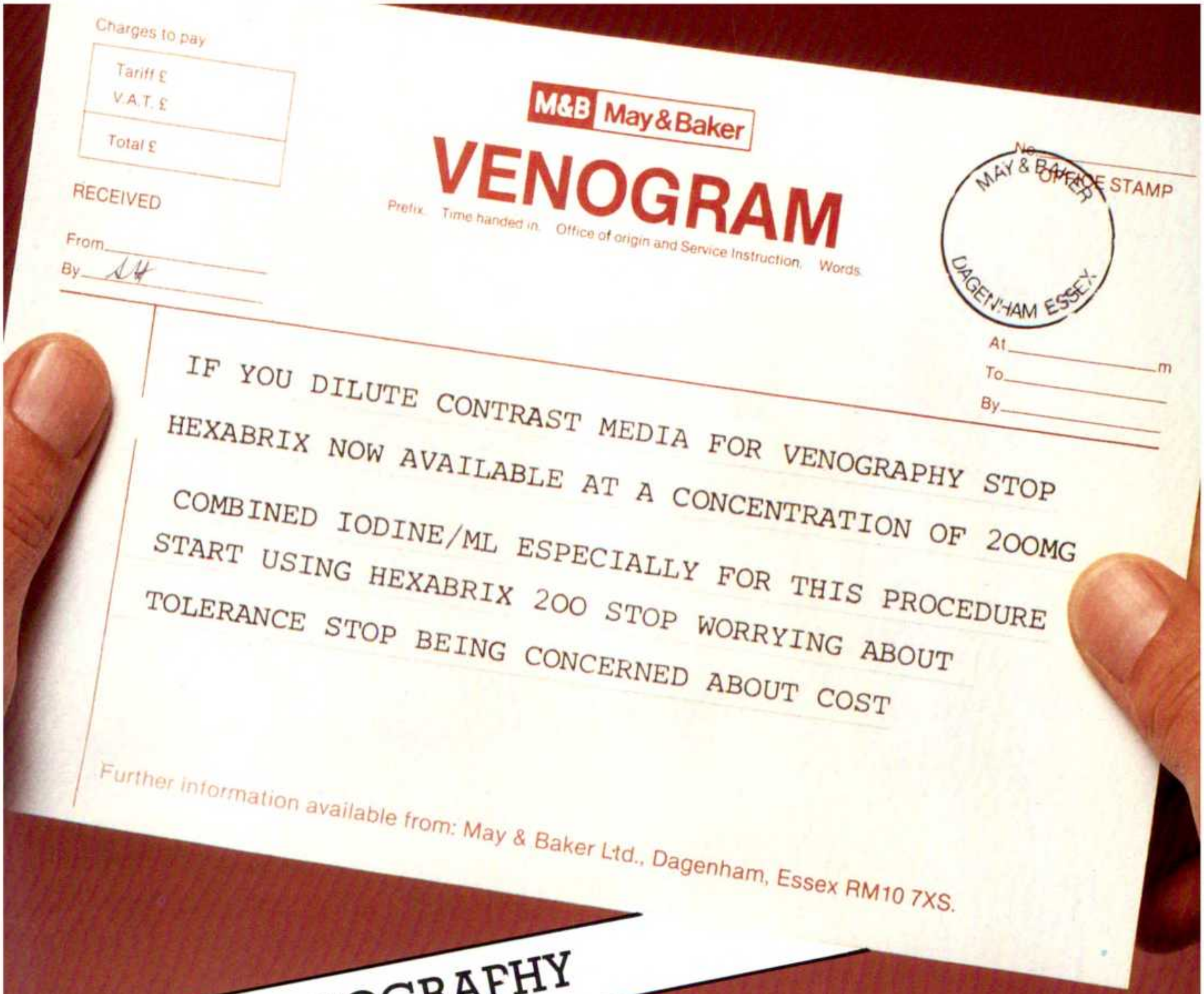

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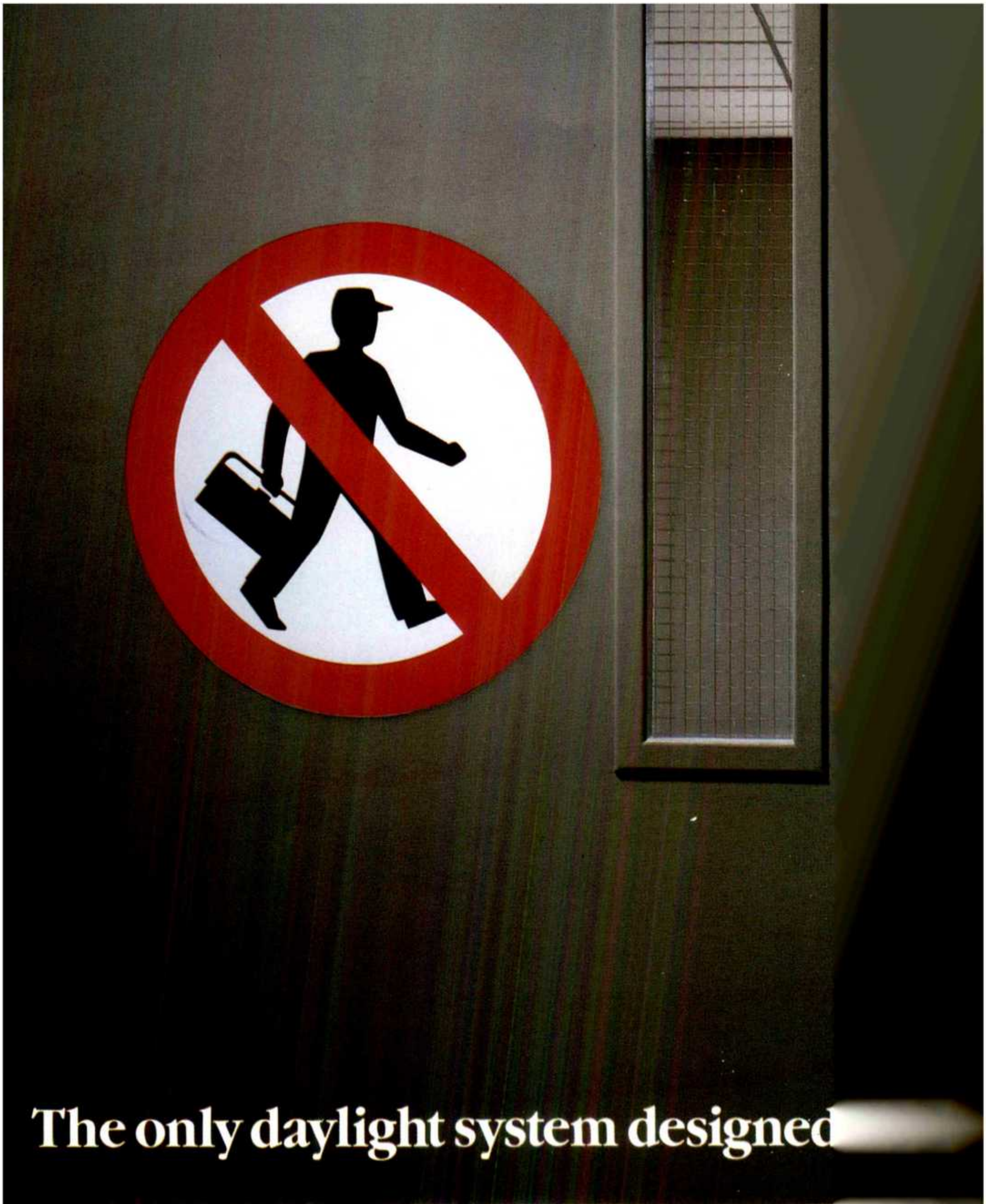

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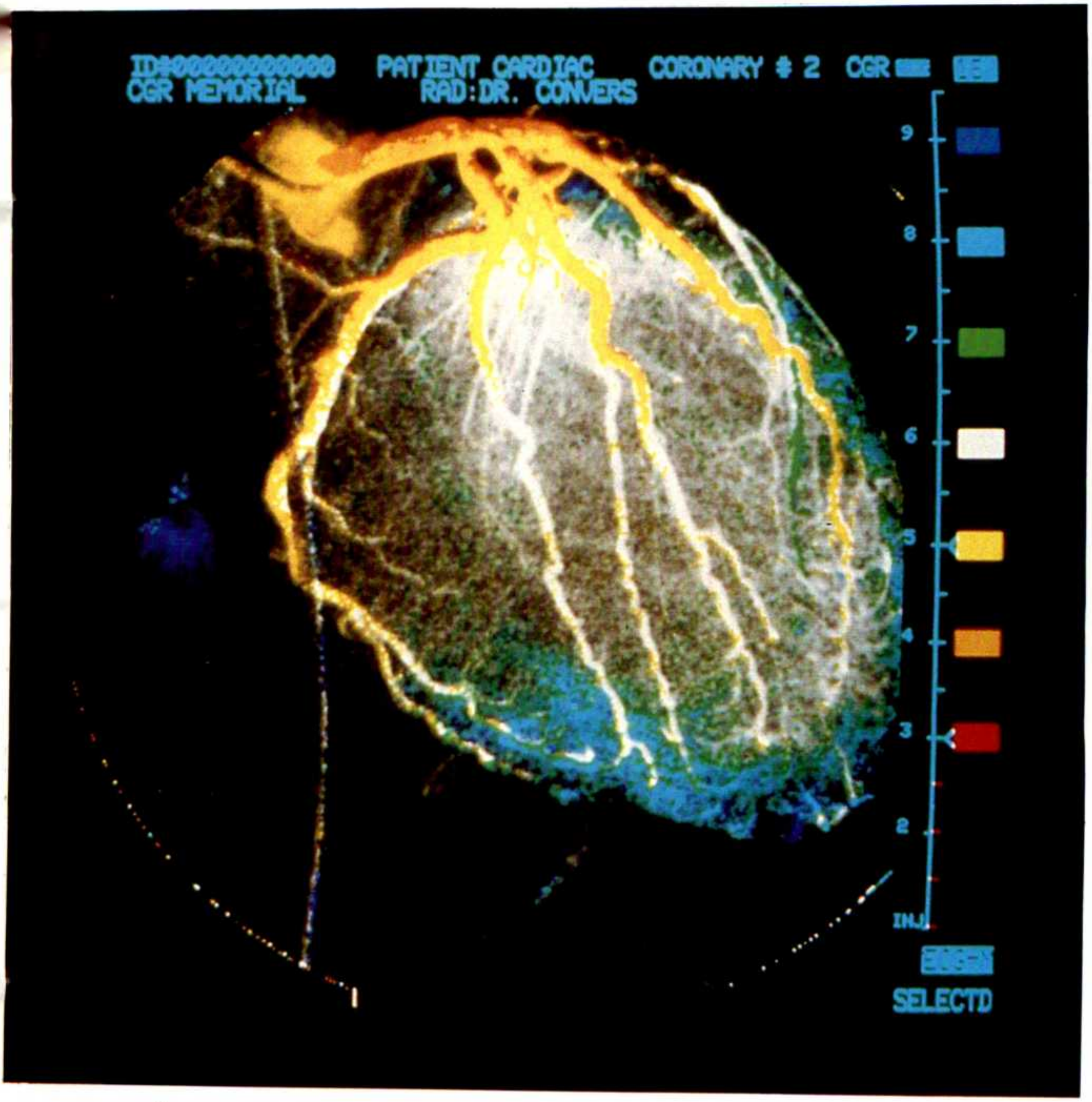

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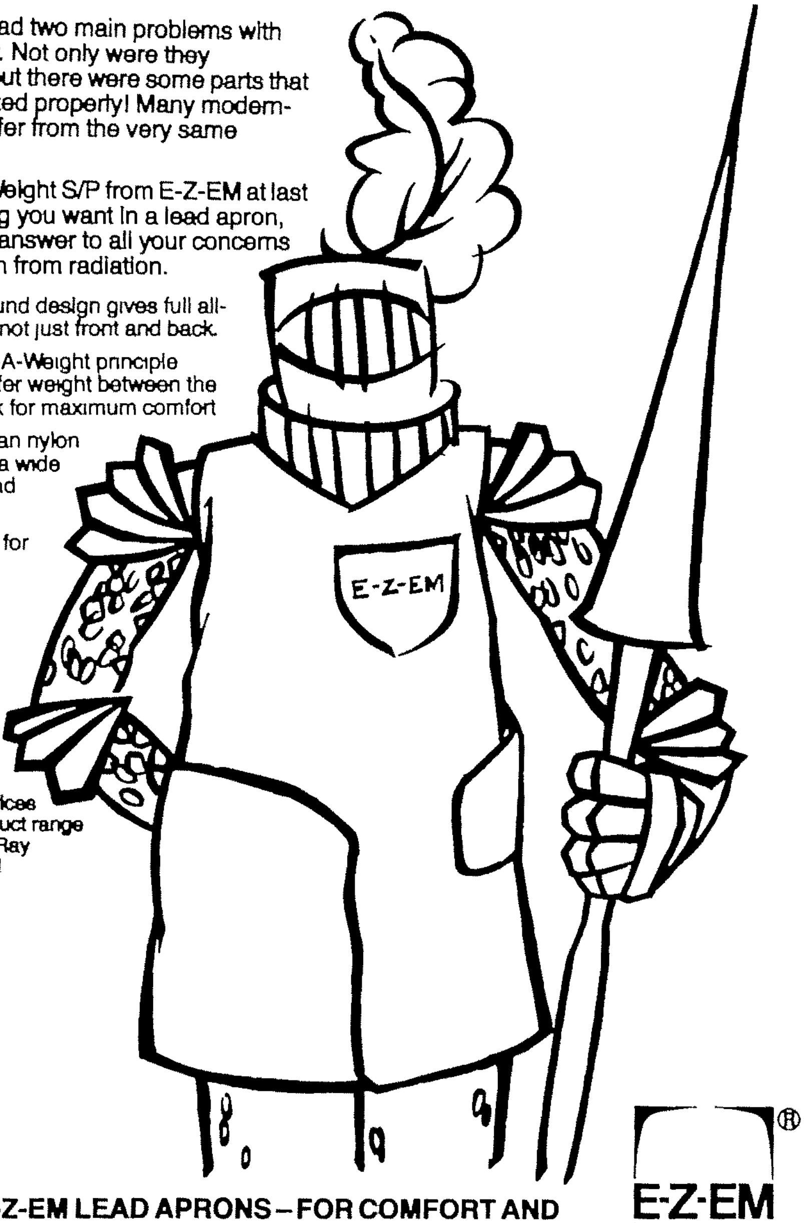

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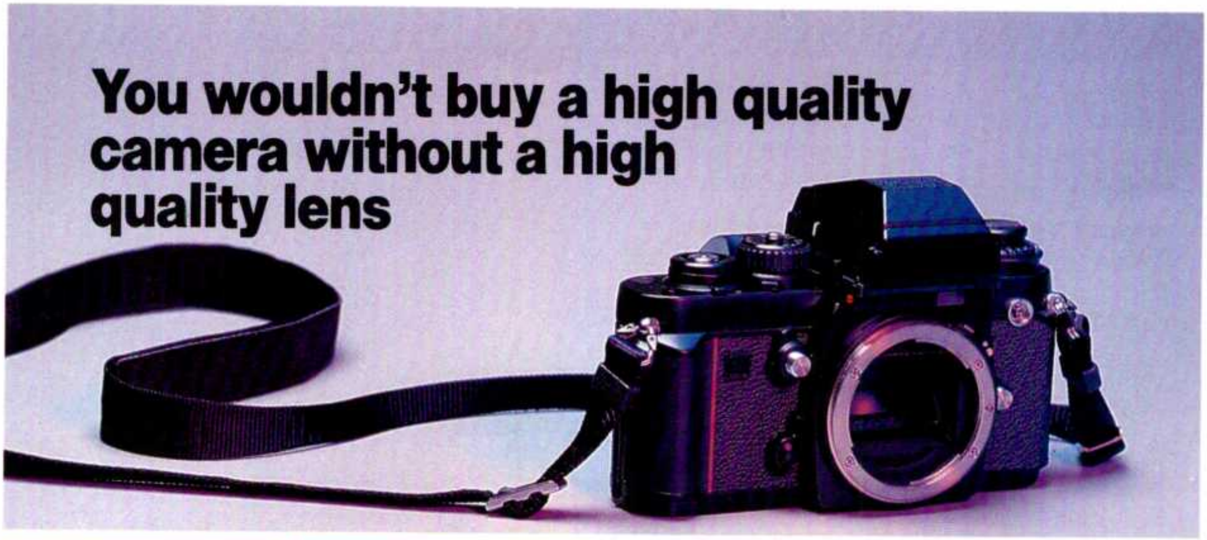
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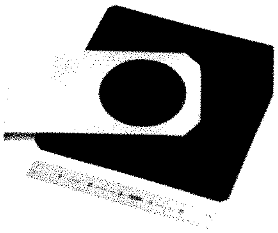

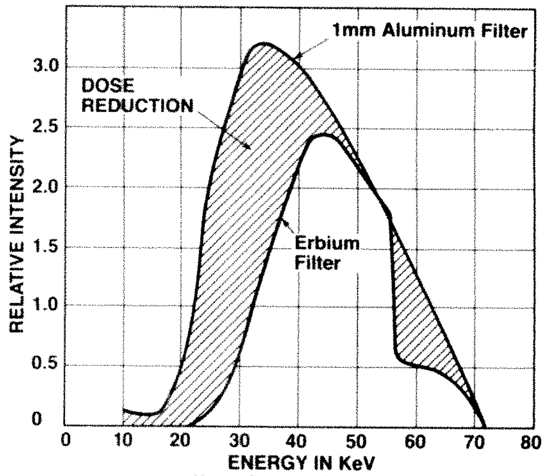

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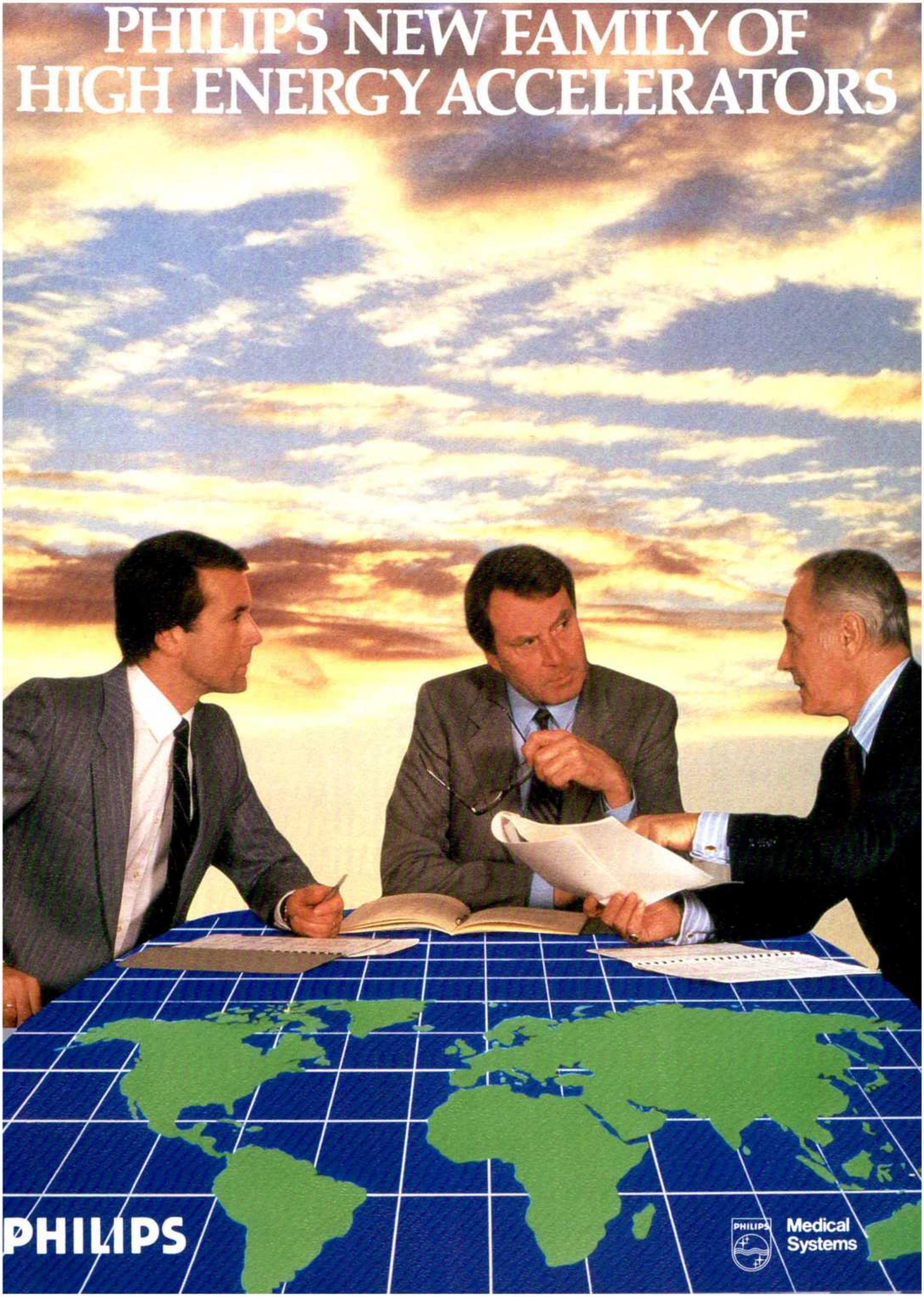
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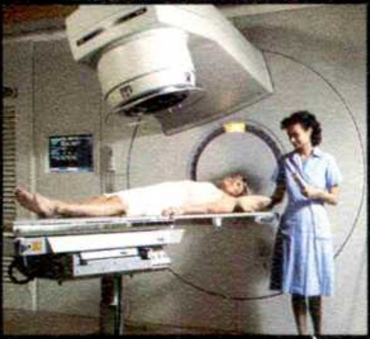

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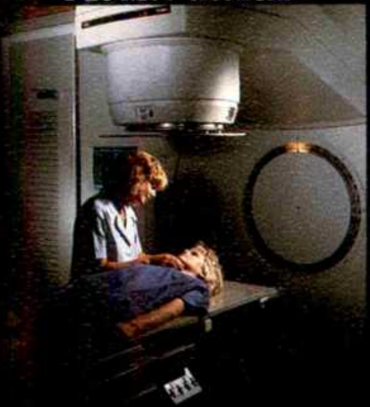

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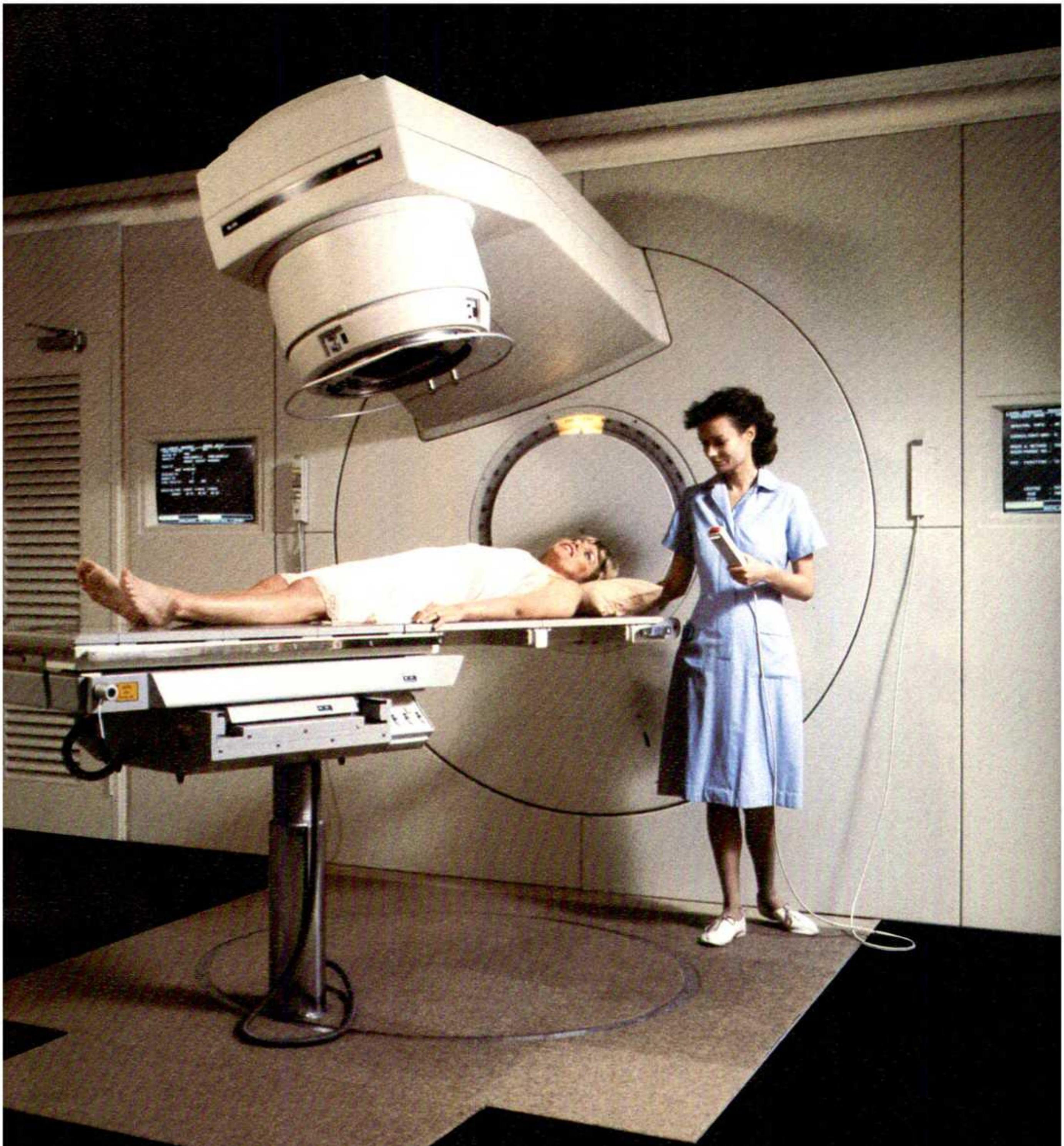

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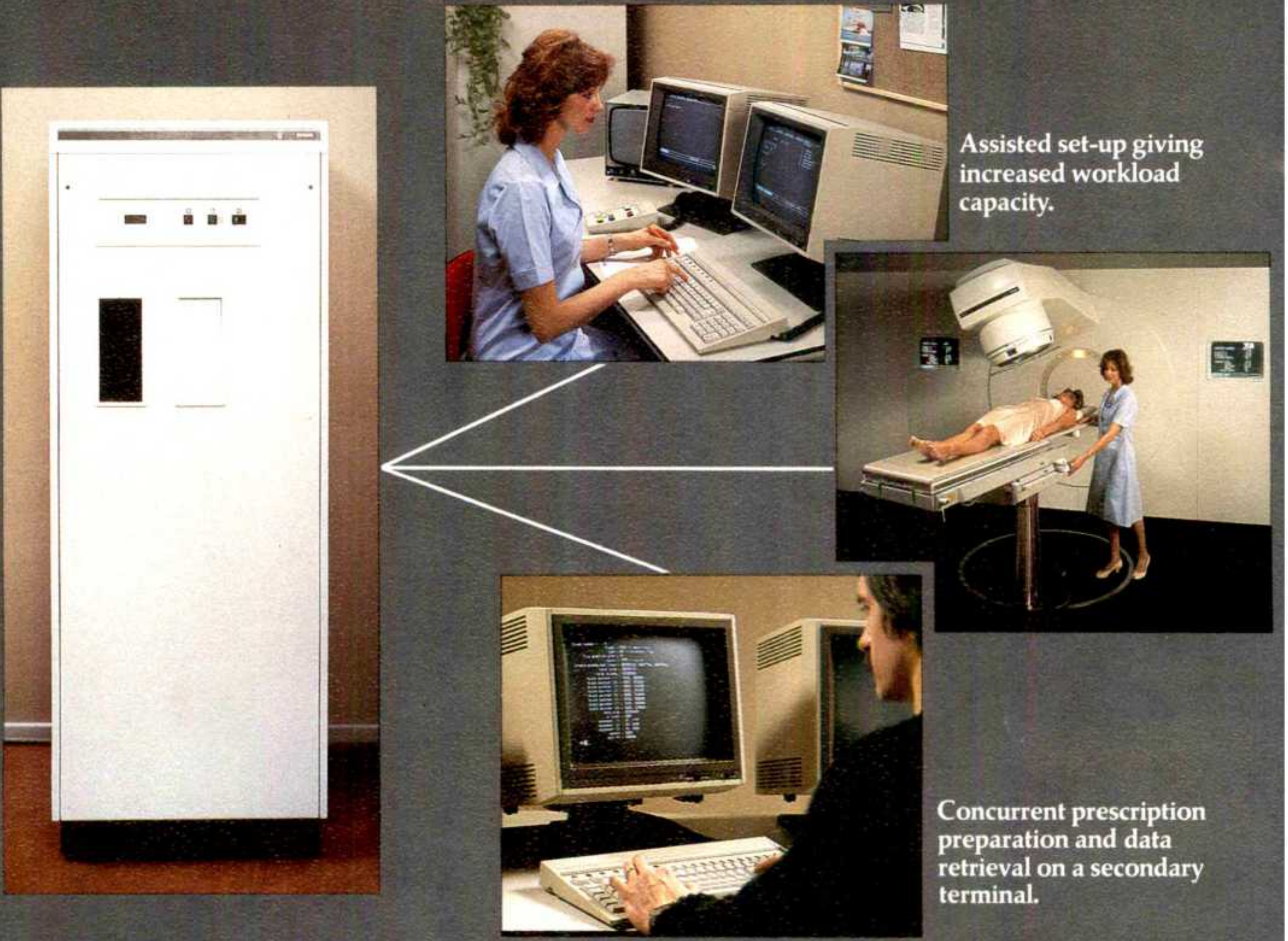

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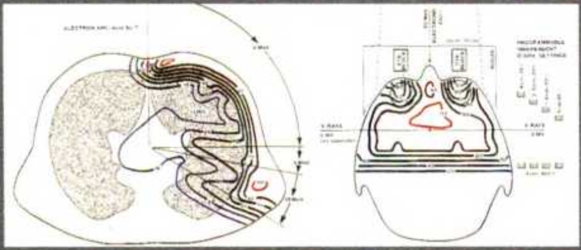

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1986, *The British Journal of Radiology*, *59*, 1057–1064
VOLUME 59 NUMBER 707 NOVEMBER 1986
The British Journal of Radiology

The sharing and computer exercising of human Know-How*

By A. d'Agapeyeff
Expertech Ltd, Slough, Berkshire

(Received April 1986)

It is, indeed, an honour for a complete outsider to medicine to have been asked to give the Mayneord Lecture at Radiology '85. It is also a privilege to have had the opportunity of meeting Professor and Mrs Mayneord and of hearing their kind reactions to a technology so recent that its entire history spans but a tiny fraction of their own contribution to medicine.

The technology in question is concerned with an instrumentation for Know-How, which is regarded as empirical human knowledge, or the compiled experience of human specialists in their domain of skill. In general this extraordinary and ancient resource, so familiar to everyone, has been lightly treated by Science and the Professions. Know-How is rarely put in written form apart from occasional fragments. Yet it is said to be the key determinant to the overwhelming majority of human decisions. However, this last is but one of many assertions on the subject which, although confidently held, is not sustained by proof. Most of the evidence about empirical knowledge is, itself, empirical.

The development of this particular technology has not been guided by cognitive science. It was originally inspired by the work of Ed Feigenbaum, who is the father of modern Expert Systems (Feigenbaum et al, 1971), but the first applications were built by British companies. The pioneers, from about 1980, included Unilever Research and the Corporate Laboratories of ICI. For various reasons the publication of these ideas was delayed until the Alvey Directorate conducted a Survey on Expert Systems in UK Industry (d'Agapeyeff, 1984). The technology only began to spread more widely with the advent of computing software tailored for the purpose, in 1985.

The relevance, or otherwise, of the current state of this technology for medical applications, has to be left to the judgment of the medical professions. The related efforts of the Biomedical Computing Unit of the Imperial Cancer Research fund (Expert Systems, 1983) does provide some encouragement. There are also activists among the Medical Specialist Groups of the British Computer Society. In this paper the technology will be described in terms of the following.

1 Some aspects of Know-How.
2 Expert Systems in medicine and business.
3 Know-How programming.
4 Some tentative conclusions.

1 SOME ASPECTS OF KNOW-HOW

In the first instance the reader's attention is drawn to the attractiveness of a well written aphorism and the recursive quality of Know-How about Know-How. Consider:

> "All knowledge is of itself of some value. There is nothing so minute or inconsiderate that I would not rather know it than not"

attributed to Dr Johnson in Boswell's "Life of Johnson", 1775.

> "Knowledge is little; to know the right context is much, to know the right spot is everything"

from the "Book of Friends" by Hugo von Hofmannsthal, 1922.

Johnson's view does seem to echo a characteristic of human curiosity. Know-How is often fascinating, providing its appreciation does not demand excessive intellectual effort. This may be a factor in the popularity of the TV programme "Mastermind" which attracts an audience of millions for no obvious reason within accepted TV scheduling lore.

Hofmannsthal is closer to the emerging creed of the self-labelled guild of Knowledge Engineers. Verbal wisdom, expressed as rules-of-thumb, is context orientated. The more specific is the rule the more direct is its applicability and the greater is its quotability (*e.g.* "if on antibiotics then try and avoid painkillers"). It is important that the expression be plausible and colloquial (analgesics is doctorspeak) but the benefits conveyed are not dependent on the degree to which any causal action is understood by either the donor or the recipient. Textbooks and training manuals do not commonly reflect the power of the quotable rough truth. The Western tradition in publications puts the emphasis on fundamental principles, logic, causal relations and justified conclusions. This is very effective in formal teaching, but it also has less fortunate consequences.

One consequence is that texts are principally devoted to relationships which hold, or are thought to hold, across different contexts, which are, therefore, excluded from the discussion. This means that readers must translate the theoretical models into those situations which are relevant to them. For many readers, the effort involved is too demanding. Another consequence is that educated persons are inclined to pretend that they reason like a machine (without the recognition of that description). This is due to a confusion between their inherited means of arriving at a decision, and its subsequent justification within the conventions of their culture. If people are asked how they solve a routine, but not too trivial, task they will tend to respond with some imagined sequence of steps which proceed logically, monotonically, and without redundancy from problem to solution. Such a sequence is a travesty of genuine human reasoning.

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*A revised and updated version of the 1985 Mayneord Lecture, delivered in Manchester on April 18, 1985 at "Radiology '85".

Know-How is a rich and redundant profusion which includes short-cut strategies, sudden jumps, zig-zag reasoning, analogies and an arsenal of tests and checks. It provides a capacity for quick decisions over a wide range of contexts. Fast, shallow reasoning from a huge collection of Know-How was, almost certainly, an indispensable requirement for the most rapacious of hunters unable to rely on physical strength. For a million years this was the basis of teaching potted knowledge and shared prejudices to the young. Its supplementation from the escalating advances of modern science is wholly beneficial. Its virtual suppression in schools, beyond the primary level, is an unnatural handicap imposed on children.

Modern life cloaks the remarkable capacity of the human brain as a knowledge store. Even with preliterate peoples it can be difficult to distinguish verbally transmitted skills from those reinforced by regular physical example. The feats of the ancient bards are suggestive. Some of their vast epics are being treated as not wholly inaccurate accounts of events which may stretch back over hundreds of years (Wood, 1985). An interesting story is told by Thor Heyerdahl on Easter Island (Heyerdahl, 1957). An islander, who claimed the skill, was persuaded to remount one of the face statues by the old methods for the first time in over 200 years. It seems that this skill had been transmitted across 11 generations without any practice. Some 30 tons of rock had to be manoeuvred via a pile of small stones and two wooden poles. The transmission may therefore have been not just a few rhyming rules but an organised "knowledge base" with feedback controls. Such an inheritance is not entirely dissimilar to latent genes. Perhaps, like the belated recognition of the importance of skin contact between mother and baby, long the practice of many tribes, there are many aspects of Know-How and its storage still ignored by educated man.

What has all this to do with medicine? An outsider must tread softly, but there may be parallels from business. Managements are slowly recognising that crucial Know-How is what distinguishes say, an award winning accountancy student from a competent, long-in-the-tooth, financial controller. Hence it is not sensible to produce procedural guidelines which only accord with the teaching of the former, while ignoring the expertise of the latter. There is now a dawning recognition that the majority of quality control and safety manuals serve no useful purpose. They are written so as to be defendable, not to be readable. They are not read, and sometimes that is just as well since they do not mirror what experts would, or should, do. There has also been one, potentially repeatable, medical experiment. Twelve general practitioners spent a weekend programming a computer from the rules of thumb they employed in diagnosing four common conditions. The outcome was a surprise. The majority agreed that the programs did approximate to their own diagnostic practices, but those programs did not correspond to anything they had ever seen in writing before at medical school or elsewhere.

2 EXPERT SYSTEMS IN MEDICINE AND BUSINESS

2.1 In the beginning

The idea of Artificial Intelligence can be dated back to the seminal work on software of Alan Turing. Turing imagined a person engaged in a conversational exchange, via a teletype, and being unable to determine whether the other party was another human or a machine—the "Turing Test" (Turing, 1938). This test has given rise to much controversy (*e.g.* the 1984 Reith Lectures) which is characterised by doubtful interpretations as to the nature of human knowledge. A stark question for these interpretations is the means by which humans handle, so readily, tasks that embody the Combinatorial Problem (*i.e* the number of alternative steps and paths to a solution are too great for any kind of exhaustive search). A curious, not to say bizarre explanation of this facility, ascribing it to human emotions, is to be found in the Lighthill Report (Science Research Council, 1973) which almost terminated UK research in Artificial Intelligence (AI) for nearly a decade.

Another explanation was assumed in the 1960s by a famous group of AI scientists at Carnegie Mellon, who sought to emulate on a computer the General Problem Solver thought to exist as a kernel intellectual function within the human brain. It proved to be another heroic journey to the end of the rainbow. Ironically, the modern explanation originated from a former student at Carnegie working on the opposite tack. Feigenbaum believed decision-making knowledge to be specific and largely the product of domain experience. He attempted to elicit this knowledge from human experts in order to build a computer program in which the knowledge was represented explicitly. Such a representation enabled the expert to participate more fully in the design, testing and interactive modification of the program. Given the co-operation of outstanding experts it was hoped to achieve the equivalent to human levels of performance from the program. This proved to be a hard task which has since been widely underestimated. Nevertheless, some very successful programs have been implemented for tasks that were otherwise intractable, and Feigenbaum's thesis on knowledge has won wide acceptance.

2.2 MYCIN and R1

The first program, following the teaching of Feigenbaum, to have made a major impact on software designs was MYCIN, a Ph.D. thesis by a subsequently qualified medical doctor (Shortliffe, 1976). MYCIN provides advice on the diagnosis of bacterial diseases of the blood together with their antibiotic treatment. It has never achieved routine usage mainly due to its prolonged dialogue. The shortest consultation takes too long for a busy physician. Nevertheless, the program did demonstrate that extensive, high-quality knowledge could be represented in a form which was intelligible and modifiable by domain experts who were not programmers.

One of the 400+ rules in MYCIN, an element of its source program, is:

IF (1) the infection is primary-bacteremia
(2) the site of the culture is a sterile site
(3) the suspected portal of entry is the gastrointestinal tract
THEN there is suggestive evidence (0.7) that the identity of the organism is bacteroides.

A fundamental feature of MYCIN is that at any point in the consultation the user can ask WHY? (*e.g.* why some question is being asked or a conclusion is being offered). MYCIN will then explain its "reasoning" in terms of the rules being obeyed. Hence, MYCIN is not like a traditional "black-box" program. The physicians remain totally responsible for the treatment of their patients. In using MYCIN they have the capability and the duty of satisfying themselves as to the validity of the reasoning, before accepting or rejecting the offered advice. Today this feature is commonly, but not universally, regarded as an essential component to an Expert System. It is routinely included in most software products for building applications.

Recently it has been the vogue to criticise MYCIN by standards which arose subsequently. This can be instructive because MYCIN is so well described in the literature (see also Buchanan & Shortliffe, 1984). Three weaknesses have emerged. Firstly, the explanations provided are not quite as good as they appear, although they are well beyond anything achieved in traditional software. There is a crucial gulf between an understandable explanation and an explained understanding. The latter requires a generic exposition and not merely reports on the detailed rules that have been, or are about to be, obeyed. Yet generics relevant to a particular user are hard to program. Secondly, MYCIN occasionally reveals an embarrassing lack of common sense. For example, the system has little appreciation of the difference between men and women or the nature of itself. In practice, mimicking an expert's full exploitation of common sense is not just hard, but currently impossible due to the sheer quantities involved. Common sense was one of the early goals of the Japanese Fifth Generation Computer Project (JIPDEC, 1980) but this has since been quietly delegated to the Sixth Generation.

The third weakness of MYCIN arises over the vexed question of the treatment of uncertainty in the knowledge. Most Expert Systems have, until recently, relied on a statistical technique of assessing probabilities (Bayes Rule) following the lead of another Californian project, PROSPECTOR (Duda et al, 1979). MYCIN employs an empirical method of combining its certainty factors (0.7 in the above example) which can be shown to be logically flawed (Adams, 1976). Nevertheless, MYCIN is said to have performed better in medical trials than theory suggests it should. A plausible explanation is that MYCIN has a shallow reasoning from good knowledge, which has the effect of limiting its mathematical flaws.

R1 is a very different system in both its design and its history. It configures customer orders for VAX and PDP-11 computers from Digital Equipment Corporation (DEC). It is the great success story among early business applications. It has saved DEC literally millions of dollars. It led directly to that company becoming the world's most experienced user of Knowledge Base Systems (DEC is believed to have 40 large applications in operation or in development). R1 was initially designed by John McDermott at Carnegie Mellon (McDermott, 1982). It is essentially simpler in approach than that advocated by the Feigenbaum school. This may have been essential to cater for the size of the DEC applications. R1 has over 5000 rules, many of which are closer to a paragraph than a sentence. However, these simplifications have caused some AI scientists to doubt whether R1 is a "proper" Expert System, and it seems to have had little stimulus on general research.

The striking simplification of R1 is that the knowledge must be treated in the program as if it were certain and precisely measured. This arbitrary requirement is not as unreasonable as the purists suppose. All branches of accountancy adopt the same convention for the excellent reason that otherwise accountancy would be still more complex and costly than it is at present. People are accustomed to such conventions which are also found in many company and hospital procedure manuals. Few are so accustomed to the subtleties of statistical algorithms which can, as a result, be a facade of precision. For example, Bayes Rule requires that the prior probabilities be assembled from independent evidence. This is ignored in most practical applications. Other simplifications in R1 are that the system only reasons forwards, without any subtle searching for the next rule, and has very limited explanation facilities. One result of these simplifications is that the DEC application building teams did not have to be, and were not, confined to those with formal training in Expert Systems.

2.3 The British experience

After the Lighthill Report (op. cit.) Expert Systems activities in the UK were kept alive chiefly by the work and the tireless teaching of Donald Michie, then

Professor of Machine Intelligence at Edinburgh University. The other big influence was lack of money so that small teams, small computers and simplifications in technique were, perforce, encouraged. One outcome was the notion of Simpler Expert Systems described in the Alvey Survey Report (op. cit.) One of these systems, British Telecom's Tracker Project, showed that the principle of human levels of performance could be softened in order to obtain modest, but useful, applications. Tracker has the aim of helping a maintenance engineer to achieve marginal improvements to his own performance in diagnosing faults in a power supply unit. The economic benefits stemmed from the marginal improvements in the serviceability of the attached telephone exchanges.

Two other categories of Simpler Expert System emerged in Britain. A group of chemists with ICI showed that it was possible to build do-it-yourself applications. They worked successfully with SPL's SAGE Expert System software, treating it as a non-programmer's programming language; a purpose for which it was not designed since such usage has not been envisaged, in print, by anyone. A group in Unilever Research hit on the notion of exploiting Expert Systems techniques in order to acquire and distribute knowledge for human consumption. This notion has been called Knowledge Communication Systems. It was quickly seen to work, and encouraged experts to write their rules of thumb hitherto confined to speech. However, the systems lacked an adequate means for the expert and the end-user to exercise the Know-How. The central importance of exercising rules of thumb only became apparent after experience with Know-How programming initiated from a synthesis of the above ideas, plus a vital contribution from the Imperial Cancer Research Fund (ICRF)

At one time it appeared that Simpler Expert Systems for Knowledge Communication would have to be confined to rules of thumb expressed with certainty. This was the prejudice wrongly put in the Alvey Survey Report from the observation that statistical quantities do not appear in colloquial advice (*e.g.* nobody, except a Californian weather forecaster, says "it is going to rain with a likelihood of 90%"). It was Mark Rogers of ICI who supplied the correction, pointing to the widespread use of gross assessments of probability (*e.g.* impossible, unlikely, unknown, likely and certain). The hurdle was a suitable method of combining these assessments in a program. The solution, so obvious once described, came from the ICRF (Fox, 1985) working toward slightly different aims.

In medicine, as in human affairs generally, the treatment of uncertainty is non-linear (*e.g.* if treatment X is potentially lethal and patient is not terminal then treatment X is not a suitable remedy). Human experts process these issues through their knowledge of the subject and the current context. Hence, it was not necessary to have an enforced quantitative calculus. Uncertainty can be programmed qualitatively, in symbolic reasoning, similar to any other aspect of the knowledge. An earlier Expert System on the diagnosis of stomach disorders was translated into a qualitative style, seemingly very effectively (*e.g.* if cholecystitis is possible and jaundice is definite then cholecystitis is probable). It was then translated, excluding the laboratory tests, from doctorspeak to colloquial English and found to be interesting and informative to both children and attenders at computing conferences.

3 KNOW-HOW PROGRAMMING

A Know-How program, or a Knowledge Communication System, is a computer program in which the knowledge is represented explicitly so that the prescribed reasoning from that knowledge can be readily exercised by both the builders and the users of the program The ability to exercise is crucial. Without it the suppliers of the knowledge may have no adequate means of recalling and refining their own rules of thumb. This is because much empirical knowledge is held below the level of immediate conscious awareness. Running the program, which may at first behave like a familiarly stupid subordinate, can act as a prompt and also aid iterative improvements in the expression of the knowledge. The same facility is equally vital for the intended end-users. The pleasure and the benefits of running a well presented Know-How program, with one's own choice of data, can be a motivation to repeat the exercise again and again. Repetition greatly contributes to the transfer of the knowledge. By contrast, humans are usually reluctant to read the best written manuals more than about twice.

The ability to exercise can be taken further. There are enormous advantages in software tools for building programs that can be employed and enjoyed by people who are not professional programmers. Anything one has done for oneself ceases to be a mystery. End-users who are able to experiment with the building of their own, small, Know-How programs quickly become a different kind of consumer for applications built by others. They have a greater appreciation of the construction, limitations and potential of these programs. Their suggestions for improvements tend to be more practical and are often phrased as draft rules

The purpose of a Know-How program thus differs fundamentally from established dogma on Expert Systems. Unlike R1, these programs do not have to do anything that is physically productive. Unlike the systems inspired by Feigenbaum, these programs are not necessarily aimed at human levels of performance and they should not, normally, be regarded as "giving advice". A preferred model is that of a parrot on your desk regurgitating bits of Know-How on demand. This is preferred because nobody would ascribe common sense to a parrot or abdicate to it their own responsibilities for a decision. These programs can still be useful while overtly incomplete and not wholly correct. For example, Expertech Ltd has an application product which is A Clarifier of Statutory Sick Pay

Regulations. The purpose of the product is to make it easier for a clerk or other person to make a claim for a typical case of staff sickness. The Department of Health and Social Security (DHSS) regulations are arranged to cope with a myriad of rare situations which cause confusion to the reader. The product contains an explicit disclaimer as to completeness or correctness, since clearly neither hold for the DHSS publications on their regulations. It is somewhat unlikely that complete correctness is ever a valid description, this side of paradise, but people will pretend to the contrary.

Purpose determines the structure and presentation of the Know-How. There is a great deal of rather effete discussion on structure within Expert Systems, much of it implying that structure is a vaguely identified property of the knowledge itself. This is a mistake. It is frequently necessary to structure the same Know-How differently in separate parts of the same application because of the differing needs of, say, a novice and an experienced practitioner in the domain. It is also important to anticipate that the novice may become less inexperienced and have needs that change after a repeated exercising of the program.

Presentation is another matter. Unlike the formal disciplines of conventional software, Know-How programs are first assembled by hacking in the rules of thumb, any old how, as they are recalled. Later the ergonomics of running the program and of receiving the Know-How has to be tackled as a distinct stage of the implementation. Good presentation is an art not a discipline. Clever designs can help the program builder juggle the presentation quickly into different forms so as to find those that achieve a suitable (subjective) response from intended users. Presentation is not just a matter of rewriting the rules. It includes a "sensible" ordering of the questions, informative reports and run-options that users subsequently decide are what was wanted.

There are several different categories of application They range from comparatively simple Clarifiers of Regulations, through the Archiving of Rare Skills to fairly comprehensive Action Guides. These will be described below, but first it is appropriate to review the boundaries of this technology

3.1 Boundaries

Advocates of the new approach in computing software, facing the normal cynicism and worse from peer groups, can fall into the habit of reciting carefully selected histories without much mention of limits to their progress. Know-How programming deserves a starker treatment. At the moment it is still in the maternity ward on a life support system of great enthusiasm from a small percentage of those engaged in computing. There are three grounds for an optimistic prognosis. Firstly, it does actually work and at low cost. Secondly, experience is accumulating rapidly which is fuelling extensions to both the programming and to practioner skills. Non-believers point to and, perhaps, exaggerate the restricted capability of current application building software, the so-called "shell" products. Be this as it may, software (like hardware) which is cheap to build and to use has a faster-rising development curve than more expensive variants.

The third item is a curious enforcer of modesty and truth. Expert System descriptions can be a marsh of clinging hype. But the success of Know-How programs is governed by the involvement of the knowledge suppliers and the reactions of the target end-users. There is, fortunately, no way currently of making propaganda an acceptable substitute for pertinent expertise. If end-users are not genuinely fascinated by a program they will obtain little or nothing from it. Practitioners quickly learn a sharp test. If sample users are so little caught up in the program that they make polite statements about it then, for some reason, the presentation of that Know-How has failed for them. If fascinated they clearly hope the questioner will go away. Equally definite are the criteria of the knowledge suppliers who may include factory foremen, maintenance fitters and more obviously prestigious experts like lawyers. If they find their involvement more difficult or less rewarding than promised, then they will announce they are too busy to continue. If the promise is fulfilled, they will often take the computer home for the weekend.

Thus it is essential to promise only what will be delivered and to be very clear as to restrictions of scope. These are set out in Table I. The list is over-modest in that, with experience, the constraints can be relaxed. Yet over-modesty can be engaging and it helps customers to show off their achievements. There is one further important limitation. An application always begins as an exploration. It is impossible to be certain in advance that the requisite Know-How can be sufficiently articulated or programmed by the existing team. The standard advice is to set a milestone after 2–4 weeks and if progress is insubstantial and there is little immediate sign of a change, then that application should be suspended.

Unfortunately, some organisations do not take this advice and continue battering their heads against a brick wall. This is made more serious by the common mistake, in organisations, of drawing too many conclusions from their initial applications. For instance, the RAF got their first application into field service within 5 weeks (Lennox, 1986) This was an amazing performance but not necessarily any guide for their next project. On the other hand, a distinguished firm of accountants failed at their first hurdle, persisted and published conclusions damning the technology. They were obviously unaware that some of their competitors have been much luckier, or wiser.

3.2 Clarifying regulations

This category of application puts into perspective the available Know-How about Know-How programs. There was no hint of it in the literature, no product was

TABLE I

KNOW-HOW PROGRAM CONSTRAINTS

These programs can be effective where:

(a) the purpose of the application is primarily to share expertise and this purpose governs the designs;

(b) the application is selected to fit the capabilities of the implementation team and their choice of software (*i.e.* the technique is not a panacea);

(c) the application is initially small and sharply focused (*i.e.* there is no doubt as to its purpose and scope);

(d) the application relies on narrow slivers of expertise confidently held by an articulate and authoritative expert;

(e) the willing involvement of the expert in the preparation of the program is sufficient to ensure that the representation of the Know-How is personal and undiluted;

(f) the structure and presentation of the Know-How is professionally arranged to fit the subjective criteria of the target end-users, preferably with the help of a sample of those users.

Notes

1 In the above, expert can be replaced by experts (plural) working together; there is then likely to be a requirement for a greater co-operation by professional Knowledge Engineers.

2 Experts differ in what they want to do for themselves. Some will not touch a keyboard while others only require a Knowledge Engineer when they are stuck. The best kind of professional support is one that meets the individual wishes of different experts without intrusion. On the other hand, (f) is usually best done by professionals.

designed for it and the pundits (such as the author) did not anticipate it. Nevertheless, it has probably become the most popular starting application in Britain attracting the attention of over 100 project teams. With hindsight the case is so obvious. Every organisation is subject to a myriad of regulations imposed by statute, by professional bodies and by management. Yet the people affected do not understand them. This is not confined to minor and boring procedures. The impression is that less than 20% of staff in most companies have any real grasp of their pension scheme. Many organisations have mandatory reporting procedures in which the assumptions at the centre, about how these reports are prepared, are not shared by those who prepare them. Similarly, there is an ocean of law attended by more cheerful ignorance than superficial acquaintance. The chief cause would seem to be a failure of communication by the regulators rather than an obtuseness on the part of those who are regulated.

These applications are usually straightforward to implement. The present situation is so bad that a first step improvement is usually achievable in 1–3 man months although much more may be required to tap the full potential of a particular application. A pension scheme can be a suitable opening experiment. It may well be too complex to do in one step, but it has natural partitions. Young employees are chiefly interested in what they pay and why. Those nearer retirement are more concerned with what they will get and when. The project can be arranged to tackle one partition at a time. Practice will extend the range of the team. A joint venture between the accounting/consultancy firm of Robson Rhodes and Expertech has produced a Clarifier on Employment Legislation. This consists of over 1000 rules and some 30 000 words of reports representing an expert's interpretation of that law, plus statutory cases, applied to different practical contexts. The application took about 4 man months to build and to polish, and runs on a common family of personal computers.

A list of sample clarifying applications is shown in Table II. There are only two main dangers that users have to be warned about in regard to these applications, namely over-ambition and over-perfection. They are not difficult projects but difficulty is relative. When starting out it is essential to aim low. A small but partial clarifier, ready soon, can be very instructive; but a Comprehensive Guide with a regularly postponed delivery date is a missed opportunity. Equally, it is necessary to be realistic about quality. People do not suddenly jump from a mess to near-perfection. A sound task for an application is to seek independent expert advice as to whether end-users could be seriously misled. This is not the same as asking whether an utter fool could fail to get the right message.

There is noise and prejudice in any Know-How program and utter fools will maltreat them, but the same is true, and worse, with human gossip. The author made the mistake of demonstrating a medical system, shown to the public and run by school children, to an audience of eminent medical statisticians. They were horrified. The rules were not in the jargon and did not have the precision of their own writing. But the public

TABLE II

SAMPLE CLARIFYING REGULATIONS APPLICATIONS BEING TACKLED

Auditing procedures
Brokerage commission rules
Car entitlements of staff
Cargo regulations
Credit approval documentation and procedures
Employment legislation
Machine room safety
Making a will
Maintenance procedures
Mandatory reporting procedures
Medical packaging requirements
Pay and allowances entitlement
Pension scheme
Personal taxation
Permitted travel and other allowances
Road barrier requirements in law
Rules for approving new products
Sales commission scheme
Sales guide
Staff loans
Staff relocation rules
Statutory sick pay

would never read that writing, despite which they would discuss and mutually diagnose their own illnesses. Experts, in their writing, can be too sensitive to peer review and they frequently exaggerate their monopoly of accepted wisdom. Hence, the briefing of those doing the checking is a matter of delicacy if serious mistakes are to be avoided in the application without effort being wasted on superfluous refinement.

3.3 Rare skills archiving

This was the earliest type of application. The present Government's economic policies have led to numerous organisations reducing their staff levels dramatically. Some have belatedly discovered that they have, in consequence, lost a great deal of expertise. With much embarrassment and no publicity, redundant specialists have been rehired, as expensive consultants, to help record slivers of their expertise. It is absolutely impossible to replace all of a person's skill, but something of value can be achieved. It is very hard to get any details on these applications, but it appears that sample projects include Know-How about special chemical additives and their substitutes, the operation and maintenance of unusual or old plant (*e.g.* refiring a blast furnace after a rapid shut-down) and, in one case, the means of varying nationally agreed piece-work schemes without disrupting labour relations. More recently, companies have become a little less secretive and a few have introduced a policy of encouraging at least some of their specialists, who are close to retirement, to archive elements of their expertise.

The category has also broadened of late. A Know-How program can be so much more fruitful than conventional flow charts or guides that the same approach is being applied to the handling of rare events and disasters (*e.g.* a head office inspection, an acquisition of a new subsidiary company or a strike). One firm, absolutely dependent on petrol for its sales and maintenance force, built a Know-How program from hindsight after failing to anticipate the results of the last national strike of petrol tanker drivers. It contained a number of obvious but easily overlooked rules of thumb; one sexist rule which lingers in memory was:

if	he has petrol
and	she does not
then	bear in mind who will be collecting the children from school.

It is characteristic of this category that it may be impossible to anticipate who will use the program, when and in what circumstances. This affects the presentation of the Know-How. In practice this varies between two extremes. There may be little contextual structure in the rules so that they are, essentially, a form of raw expertise which may serve as a background briefing for a future user. Alternatively, there may be a range of contexts so as to provide the unknown user with greater clarity as to the implications of, and the justification for, the stored expertise. Both may be advantageous where the user has a serious need for, and really does not possess, that expertise. However, this type of application works less successfully as an enhancer of existing skills because the latter requires the user's needs to be closely anticipated.

3.4 Action guides

These guides stretch from little more than an archived skill (*e.g.* how an expert performs a particular set of tasks) to something that is not far from a full-scale adviser, albeit with end-users still responsible for their own decisions. In business these applications are often regarded as being of potential competitive importance so that little is revealed as to their progress. Once again it is advisable to start with modest goals which may be broadened after earlier success. One application that is attracting substantial investment is branch banking guides. The banks have the problem, shared by other big organisations, that they provide an increasing array of services (*e.g.* insurance, investments and mortgages), each of which has its own specialists in central and regional offices. However, the opportunity for sales includes everyday contact of branch staff with customers. Few branches can have specialist staff for any particular service so there is a problem of how to help, say, a Cotswold branch sell insurance to a sheep farmer.

It is no secret that the senior managers of the London Clearing Banks have been disappointed by the sales performance of their banches for years. They do run seminars, but the primary medium of internal briefing is paper. The branches tend to have an awesome pile of paper, no doubt full of good stuff, but it is unrealistic to suppose it serves much purpose. It is possible that a carefully prepared library of Know-How programs could be made attractive to use, could build up the confidence of branch staff in their grasp of what should be sold to whom and through personal practice on the computer, help to make them feel comfortable in their ability to offer a sales pitch to long-standing customers.

One snag about such plans (which in a different form also arises in the capture of the unwritten maintenance expertise in large engineering plants) is that of the threshold level of necessary Know-How. If a user department already has lots of personal computers then small applications may be distributed for occasional use. But if a new aid is being introduced for regular use, then it may require its own dedicated computers and will often need to be on a certain scale before that aid is meaningful. There can then be a "Catch 22" situation. No manager may be willing to confirm the development of the entire threshold level of applications without field trial results of the first projects, but adequate field trials may not be possible without that full set of applications.

Fortunately, a way out of this kind of dilemma has begun to emerge. In practice, a Know-How program will rarely leave an internal regulation or written guide undisturbed. There are two main reasons. Firstly, the management find it easier to exercise the program for themselves than read the relevant printed material. They are often disturbed by what they find and tend to order a change to the program. Secondly, most experts find the exercising of their Know-How causes them to obtain a better grasp of it as a whole and to modify what they would do in future. For example, the software may include a Knowledge Checker looking for errors and inconsistencies in the rules. This extends what a human can do by introspection alone. It is not yet accepted by all companies, but the programming of Know-How should always produce improvements that alone may make the effort worthwhile.

4 Some Tentative Conclusions

The big surprise for those working in this field is not the imperfections in current tools and techniques. It is that the very idea of instrumenting Know-How for human consumption has to be defended against vigorous attack. Those who have never seen an effective Know-How program frequently have little hesitation in dismissing its basic tenets. Even polite critics continue to raise issues that experience has largely resolved. For example, the socially aware are inclined to debate endlessly whether human experts will co-operate with an elicitation of their knowledge. The repeated experience that experts can be intrigued, but not ordered, into co-operation has little impact on such debates. The observation that for centuries enormous investments in time and money have been put into teaching and training material which ignores Know-How, is received in stony silence. In seminars at Expertech, over 500 large organisations have been challenged to identify a quality control or safety manual that embodies, readably, the verbal wisdom of their respected specialists. No response has ever been received to this challenge.

The essential difficulty is flatly contradictory interpretations of reality. This was clarified by one particular vigorous series of exchanges. The lethal thrust was to the effect that there could be no assurance that a given program was not built from prejudice. This met the parry that, on the contrary, there was absolute assurance. All effective Know-How programs were composed of prejudice from experience which constituted the source of their power The result of the exchanges was a state of mutual incomprehension.

On the other hand, there are enthusiasts who herald an impending renaissance in which instrumented Know-How is balanced with scientific truth in the recognised arsenal of decision-making knowledge accessible to human beings. If this should come about it will not be due to the sudden marvels of any computing software, but it just might be a reaction to the careless treatment of Know-How hitherto.

The question for medicine is similar to that of every profession. Should medical Know-How be left to verbal guidance alone? If not, how may it best be represented and exploited? The author is but a patient with a family of patients. Their interest is obvious. It is that authorised and exercisable medical Know-How be made available, as widely as possible, as a replacement for much gossip and as a supplement to the advice of overworked general practitioners. A final conclusion is that if this commodity is not supplied by physicians then the market need of patients will be met from commercial ventures, with whatever risks and benefits may flow from such an outcome.

REFERENCES

Adams, J B., 1976 A probability model of medical reasoning and the MYCIN model. *Mathematical Biosciences, 32.*

BCS Specialist Group on Expert Systems *Proceedings of Expert Systems 83*

Buchanan, B G & Shortliffe, E., 1984. *Rule Base Expert Systems The MYCIN Experiments of the Stanford Heuristic Programming Project* (Addison Wesley 0201 10172)

d'Agapeyeff, A., 1984. *A Survey on Expert Systems in UK Industry* (The Alvey directorate, London).

Duda, R , Gashing, J. & Hart, P., 1979. Model design in the Prespector Consultant System for mineral exploration In *Expert Systems in the Microelectronic Age.* Ed by D Michie (Edinburgh University Press).

Feigenbaum, E A , Buchanan, B. J. & Lederburg, J., 1971 On generality and problem solving: a case study using the dendral program *Machine Intelligence, 6.*

Fox, J , 1985 Coping with Uncertainty. *The Alvey Lectures* (Harper and Row).

Heyerdahl, T , 1957 *Aku Aku The Secret of Easter Island.* (George Allen and Unwin, London).

JIPDEC, 1980 *Interim Report on Study and Research on Fifth Generation Computers* (The Japanese Information Processing Development Centre, Tokyo).

Lennox, J., 1986 Experts get down to brass tacks *PC World,* March 18

McDermott, J., 1982. "R1: a rule based configurer of computing systems. *AI Journal, 19,* No. 1.

Science Research Council, 1973. *Artificial Intelligence A Paper Symposium*

Shortliffe, E., 1976. *Computer-based Medical Consultations MYCIN* (Elsevier, New York).

Turing, A , 1938 Computing machinery and intelligence. Reprinted in *Minds and Machines* Ed. by A. Anderson (Prentice-Hall, New Jersey), 1964

Wood, M , 1985 *In Search of the Trojan War* (Guild Publishing, London)

1986, *The British Journal of Radiology*, 59, 1065–1068 NOVEMBER 1986

Ossification centre of the hyoid bone in DiGeorge syndrome and tetralogy of Fallot

By Theadis R. Wells, H.T. (A.S.C.P.), *Vicente Gilsanz, M.D., *Melvin O. Senac Jr, M.D., Benjamin H. Landing, M.D., *Linda Vachon, M.D. and †Masato Takahashi, M.D.

Departments of Pathology, *Radiology and †Pediatrics (Cardiology Division), Childrens Hospital of Los Angeles and USC School of Medicine, USA

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ABSTRACT

The incidence of radiographic visibility of the ossification centre of the body of the hyoid bone in radiographs taken during the first month of life was analysed for 34 autopsied infants: 16 with DiGeorge syndrome (DGS), 14 with tetralogy of Fallot (TOF), four with interrupted aortic arch (IAA) and a further 13, surviving infants with non-DGS TOF or non-DGS IAA. The incidence of visible hyoid ossification centre (HOC) was 75.7% in a control series of infants with neither congenital heart disease (CHD) nor DGS. Autopsied patients with DGS, TOF without DGS, and IAA without DGS showed a significantly low incidence of visible HOC. Infants with TOF (and possibly those with IAA) who did not have DGS and who did not die during infancy showed a normal incidence of visible HOC in radiographs taken during the first post-natal month. Radiological visibility of the HOC in the first post-natal month appears useful in the diagnosis of DGS and forms of CHD often seen in association with DGS and in assessing prognosis of neonates with certain types of CHD.

The DiGeorge syndrome (DGS; III–IV pharyngeal pouch syndrome) includes absence of the thymus and parathyroid glands (derivatives of third and fourth pharyngeal pouches) in complete DGS and hypoplasia of either or both the thymus and parathyroid glands in partial DGS. Congenital heart disease (CHD) is a frequent feature of DGS, with Type B interruption of the aortic arch (IAA) a distinctive finding (Moerman et al, 1980; Van Mierop & Kutsche, 1984; Ferry & Hohn, 1985; Wells et al, 1986); the aortic arch is a derivative of the fourth branchial arch, which lies between the third and fourth pharyngeal pouches in early fetal life.

Recent studies of the thyroid cartilage (a derivative of the fourth branchial arch) have found reduced size and retarded maturation of this cartilage in DGS, and also in patients with tetralogy of Fallot (TOF) suspected but not proven to have DGS (Wells et al, 1986). Although some authors describe the hyoid bone, a derivative of the second and third branchial arches, as ossifying from six centres, two in the body and one in each of the greater and lesser cornua, the youngest fetuses we have studied have had only one ossification centre in the body, suggesting that, if there are two centres in the body of the hyoid in early fetal life, they fuse shortly after forming, as is also the case, for example, in the basi-sphenoid. For this reason, in this paper we refer to ossification of the body of the hyoid as being from one centre. It is usually the first centre of the hyoid which becomes visible radiographically. Since the third branchial arch is immediately cephalad to the third pharyngeal pouch, the present study was conducted to establish whether abnormality of the hyoid bone also occurs in DGS and TOF. We have found no prior reports of specific association of radiographically demonstrable hyoid-bone abnormalities with congenital heart disorders or other malformation syndromes.

PATIENTS AND METHODS

Chest radiographs, either lateral or antero-posterior (AP) views, with the head rotated to one side (Fig. 1), of 34 autopsied infants with CHD who had radiographs taken before age 1 month at Childrens Hospital of Los Angeles (the autopsy series), were reviewed for visibility of the ossification centre in the body of the hyoid bone. Comparable radiographs of 37 neonates without CHD or DGS were also reviewed (the radiology control series).

The incidence of radiologically visible hyoid ossification centre (HOC), sex and mean age of the patients in each group at the time of radiography are presented in Table I and Fig. 2 for the following groups of patients: 16 patients with DGS, 14 autopsied patients with TOF but without DGS and four autopsied patients with IAA but without DGS. The data for these categories of patients were compared with a control group, consisting of 37 neonates of comparable age who had neither DGS nor CHD, from the Radiology Department files. The findings in the autopsied patients with non-DGS TOF (14 patients) and non-DGS IAA (four patients) were also compared with those of radiographs taken during the first month of life of neonates with these same conditions who have not died (the cardiology series). These data are also presented in Table I and Fig. 2, with the results of statistical analysis (χ^2) of the distributions observed. Student's *t*-test was used to

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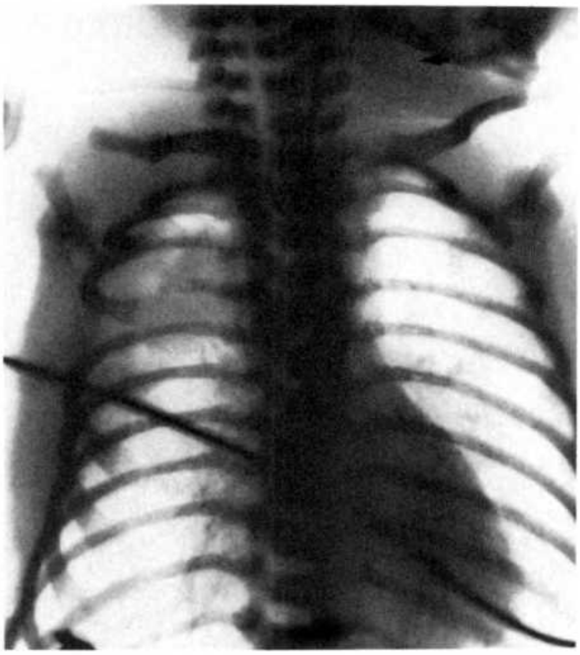

Fig. 1.

Antero-posterior chest radiograph of 11-day-old male infant showing complete DGS with non-visibility of the HOC (arrow).

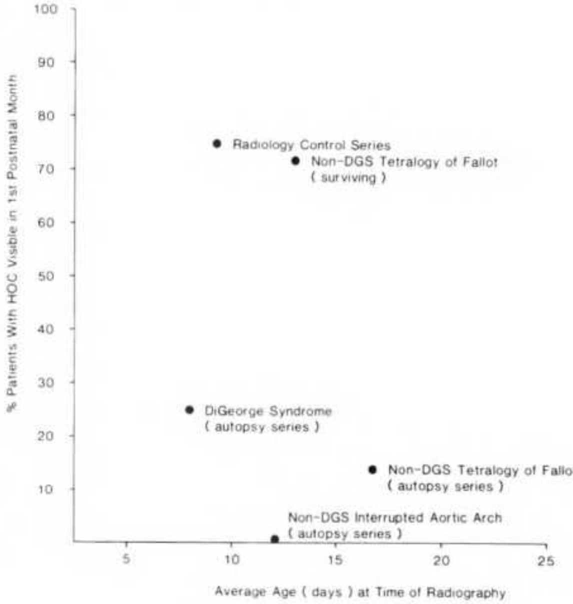

Fig. 2.

Relationship of the incidence of radiographically visible HOC in various groups of patients to the average age (days) at the time of radiography, showing significantly reduced visibility of HOC in autopsied patients with DGS, non-DGS TOF and non-DGS IAA, compared with the value in the radiology control series. The incidence of radiologically visible HOC is also normal in surviving infants with non-DGS TOF.

evaluate differences in length of survival of patients with partial versus complete DGS.

Results

The incidence of radiographically visible HOC in neonates 1 month of age or less at the time of radiological examination was 75.7% in the radiology control series. No difference between the sexes was apparent. The earliest gestational age at which the HOC was visible in the radiology control series of this study was 29 weeks.

Patients with DGS had a reduced incidence of visible HOC in radiographs taken during the first post-natal month, compared with the radiology control series ($4/16 = 25\%$ vs $28/37 = 75.7\%$, $p < 0.01$; complete DGS, $0/5 = 0\%$; partial DGS, $4/11 = 36\%$) (Table I). The non-DGS TOF infants from the autopsy series also showed a low incidence of visible HOC ($2/14 = 14\%$) in radiographs taken within 1 month after birth, as did the four patients with non-DGS IAA from the autopsy series, none of whom had visible HOC on radiographs taken during the first month. In contrast, eight of 11 infants with non-DGS TOF who did not die in infancy had radiographically visible HOC during the first post-natal month (72.7%), as did the two infants with non-DGS IAA who did not die in infancy.

Infants with partial DGS who died lived significantly longer (age at death 72.6 ± 89.6 days, $p < 0.05$) than did patients with complete DGS (18.1 ± 14 days).

Six of the 34 autopsied patients (18%) with DGS, non-DGS TOF, or non-DGS IAA (four females and two males) were hispanic (three), black (two) or oriental (one). The incidence of visible HOC in these patients was 1/6 (17%), *i.e.* no ethnic effect on this feature was apparent, a finding of interest since blacks and orientals have been reported to have earlier appearance of appendicular skeleton ossification centres than caucasians (Durham et al, 1939; Christie, 1949; Garn et al, 1967; Pryse-Davies et al, 1974).

Discussion

Hyoid ossification normally begins in the fifth month of gestation (Hill, 1939), and at term the centre in the body of the hyoid bone is radiographically demonstrable in 75% of neonates (Tompsett & Donaldson, 1951). In lateral projection, its shape varies from that of a triangle with the base posterior to that of a half-ellipse with the convexity anteriorly. The centre is visible at the level of the second to third cervical vertebrae in lateral radiographs, and also in AP chest views of many infants, especially if the head is rotated to one side.

TABLE I

INCIDENCE OF VISIBILITY OF THE HYOID OSSIFICATION CENTRE IN RADIOGRAPHS TAKEN DURING THE FIRST POST-NATAL MONTH, FOR PATIENTS WITH DIGEORGE SYNDROME, AND TETRALOGY OF FALLOT OR INTERRUPTED AORTIC ARCH WITHOUT DIGEORGE SYNDROME

	No. of patients	Incidence of visible HOC	χ^{2}*
Tompsett and Donaldson (1951)	500	376/500 = 75.2%	
Controls (non-CHD) (F = 13; M = 24)	37	28/37 = 75.7%	
DiGeorge syndrome (F = 9; M = 7)	16	4/16 = 25.0%	+ < 0.01
(partial	11)	4/11 = 36.0%	
(complete	5)	0/5 = 0%	
Tetralogy of Fallot (non-DGS), fatal (F = 9; M = 5)	14	2/14 = 14.0%	+ < 0.01
Interrupted aortic arch (non-DGS), fatal (F = 2; M = 2)	4	0/4 = 0%	
Tetralogy of Fallott (non-DGS), not fatal (F = 5; M = 6)	11	8/11 = 72.7%	NS
Interrupted aortic arch (non-DGS), not fatal	2	2/2 = 100%	
Total, this series	84		

The oldest autopsied patient with non-DGS TOF was aged 2 years 6 months (group mean age = 5.27 months); the youngest surviving patient with non-DGS TOF was aged 2 years 3 months (group mean age 5 years 4 months) ($p < 0.001$).
*Probable significance. NS = not significant.

Tompsett and Donaldson (1951), in the study referred to above, showing radiographic visibility of the HOC in 75% of normal neonates, found no difference between the sexes. The latter observation, which is supported by the data in this report, is of interest in view of the well known sex difference in ossification-centre appearance for the appendicular skeleton, with earlier appearance in females (Pryor, 1923; Durham et al, 1939; Christie, 1949; Pryse-Davies et al, 1974).

The high association of DGS (partial and complete) with TOF (all forms) (Rose et al, 1974; Moerman et al, 1980; Wells et al, 1986), the abnormally small thyroid cartilage seen in DGS and in patients with TOF suspected of having DGS (Wells et al, 1986), and the abnormally low incidence of visible HOC in radiographs taken during the first post-natal month for patients with DGS and non-DGS TOF are consistent with a proposal that the cause(s) or mechanism(s) of DGS and of TOF have elements in common. Reduced radiographic visibility of HOC in autopsied patients with IAA, a lesion also associated with DGS (Conley et al, 1979; Moerman et al, 1980; Van Mierop & Kutsche, 1984; Ferry & Hohn, 1985; Wells et al, 1986), was also found.

Of interest was the normal incidence of visible HOC (72.7%) in radiographs taken during the first month of life of patients with non-DGS TOF who did not subsequently die, compared with the low value (14%) for the non-DGS TOF patients who did die. Reduced visibility of HOC in autopsied patients with non-DGS TOF does not seem to be due to reduced gestational age or multiparity, as only two patients in this study with non-DGS TOF were premature and only one (born at term) was a twin. The differences in the incidence of visible HOC in the first month of life between the two populations of TOF may suggest that there are two biological types of TOF.

Two infants with non-DGS IAA who survived after surgical correction (cardiology series) of the lesion had radiographically visible HOC, while all four patients with non-DGS IAA who died in early infancy did not. The possibility that radiographic visibility of the HOC in a neonate with TOF or IAA implies a better prognosis would appear to merit further study.

The finding that the infants in the study with partial DGS live significantly longer ($p < 0.05$) than those with complete DGS is of interest. Calculations from the data of Conley et al (1979) show a similar difference ($p < 0.05$) in duration of survival for patients with partial DGS versus those with complete DGS. The data from the present study suggest that partial DGS is the most probable diagnosis for an infant diagnosed as having DGS who survives beyond about 32 days (mean + 1 SD for complete DGS) without specific treatment.

REFERENCES

CHRISTIE, A. U., 1949. Prevalence and distribution of ossification centers in the newborn infant. *American Journal of Diseases of Children, 77,* 355–361.

CONLEY, M. E., BECKWITH, J. B., MANCER, J. F. K. & TENCKHALL, C., 1979. The spectrum of the DiGeorge syndrome. *Journal of Pediatrics, 94,* 883–890.

DURHAM, E. C., JENSS, R. M. & CHRISTIE, A. U., 1939. A consideration of race and sex in relation to the growth and development of infants. *Journal of Pediatrics, 14,* 156–160.

FERRY, D. A. & HOHN, A. R., 1985. Interrupted aortic arch. *Journal of Perinatal Medicine, 5,* 70–71.

GARN, S. M., ROHMANN, C. G. & SILVERMAN, F. N., 1967. Radiographic standards for postnatal ossification and tooth calcification. *Medical Radiography and Photography, 43,* 45–66.

HILL, A. H., 1939. Fetal age assessment by centers of ossification. *American Journal of Physical Anthropology, 24,* 251–272.

MOERMAN, P., GODDEERIS, P., LAUWERIJNS, J. & VAN DER HAUWAERT, L. G., 1980. Cardiovascular malformations in DiGeorge syndrome (congenital absence or hypoplasia of the thymus). *British Heart Journal, 44,* 452–459.

PRYOR, J. W., 1923. Differences in the time of development of centers of ossification in the male and female skeleton. *Anatomical Record, 25,* 257–273.

PRYSE-DAVIES, J., SMITHAM, J. H. & NAPIER, K. A., 1974. Factors influencing development of secondary ossification centres in the fetus and newborn. *Archives of Disease in Childhood*, *49*, 425–431.

ROSE, J. S., LEVIN, D. C., GOLDSTEIN, S & LASTER, W., 1974. Congenital absence of the pulmonary valve associated with congenital aplasia of the thymus (DiGeorge's syndrome). *American Journal of Roentgenology*, *122*, 97–102.

TOMPSETT, A. C. & DONALDSON, S. W., 1951. The anterior tubercle of the first cervical vertebra and the hyoid bone: their occurrence in newborn infants. *American Journal of Roentgenology*, *65*, 582–584.

VAN MIEROP, L. H. S & KUTSCHE, L. M., 1984. Interruption of the aortic arch and coarctation of the aorta: pathogenetic relations. *American Journal of Cardiology*, *54*, 829–834.

WELLS, T. R., LANDING, B. H., GALLIANI, C A. & THOMAS, R A., 1986 Abnormal growth of the thyroid cartilage in the DiGeorge syndrome and in tetralogy of Fallot. *Pediatric Pathology*, in press.

1986, *The British Journal of Radiology*, 59, 1069–1072 NOVEMBER 1986

Ossification centre of the hyoid bone in complete transposition of great vessels, Ivemark asplenia syndrome, and Down's syndrome with congenital heart disease: correlation with the humeral capital epiphysis

By Theadis R. Wells, H.T. (A.S.C.P.), Benjamin H. Landing, M.D., * Melvin O. Senac Jr, M.D. and *Vicente Gilsanz, M.D.

Departments of Pathology and *Radiology, Childrens Hospital of Los Angeles and University of Southern California School of Medicine, USA

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ABSTRACT

The incidence of radiographic visibility of the ossification centres of the body of the hyoid bone and of the humeral capital epiphysis in antero-posterior or lateral chest radiographs taken during the first month of life of 63 autopsied infants were analysed. The group comprised patients with Down's syndrome (DS) with congenital heart disease, 15; complete transposition of the great vessels (TGV), 10; Ivemark asplenia syndrome (IS), 17; and a control group of infants with congenital heart disease (CHD) who had none of the above conditions, nor tetralogy of Fallot, interrupted aortic arch, DiGeorge syndrome or hypoplastic left-heart complex, 31. The incidence of radiographically visible hyoid ossification centre (HOC) in the control group was 71% and of humeral capital epiphysis (HE), 16.1%. Autopsied infants with TGV, IS or DS with CHD showed increased visibility of HOC (100%); the incidence of visible HE was increased in neonates with IS (71.4%) and with TGV (50%). The differences in the incidence of radiographic visibility of HOC and HE in neonates with CHD, in this study and in others in the literature, appear to have diagnostic value.

The specific diagnosis of congenital heart disease (CHD) by chest radiography, of a newborn infant is frequently difficult as there are few specific findings. The ossification centre of the body of the hyoid bone, a derivative of the second and third branchial arches, is radiologically visible in approximately 75% of normal-term neonates. Recent studies have shown a significant decrease in incidence of visibility of the hyoid ossification centre (HOC) in infants with DiGeorge syndrome and tetralogy of Fallot (Wells et al, 1986). Presence or absence of a visible HOC may thus aid in the specific diagnosis of CHD in a neonate. The present study was designed to investigate the incidence of radiologically visible ossification of the hyoid bone and humeral capital epiphysis (HE) in radiographs of infants with different types of CHD taken during the first post-natal month.

MATERIALS AND METHODS

The incidence of visible HOC and HE was determined from chest radiographs, either lateral or antero-posterior (AP) views with the head rotated to one side (Fig. 1), of 32 autopsied infants with CHD, who had chest radiographs taken during the first post-natal month. The diagnoses of these infants were Down's syndrome (DS) with CHD (15); complete transposition of great vessels (TGV) (10), and Ivemark asplenia syndrome (IS) (7). Comparable data for a control group of 31 autopsied infants with CHD who had none of the conditions listed above, nor tetralogy of Fallot (TOF), interrupted aortic arch (IAA), DiGeorge syndrome (DGS) or hypoplastic left-heart complex, were also obtained (the autopsy control series). Age at the time of radiography, sex and ethnic group were also noted. The radiographs of all 63 autopsied infants in this report are in the files of the Gabrial C. Duque Jr Memorial Cardiac Registry of the Pathology Department, Childrens Hospital of Los Angeles.

The incidence of radiographically visible HOC and HE, the ratio of % HOC visible/% HE visible for the various groups of patients and the mean age of the patients in each group at the time of radiography are presented in Table I and Fig. 2, with the results of statistical analysis (χ^2) of the distributions observed.

RESULTS

Hyoid ossification. The incidence of radiographically visible HOC in neonates 1 month of age or less at the time of radiological examination was 71% in the autopsy control series, with no difference between the sexes. The earliest gestational age at which the HOC was radiographically evident in the autopsy control series was 36 weeks. Infants with complete TGV, IS or DS with CHD had an increased incidence of visible HOC in radiographs taken during the first month of life, compared with the autopsy control series (100% versus 71%), as shown in Figs 2 and 3.

Humeral capital epiphysis. The incidence of visibility

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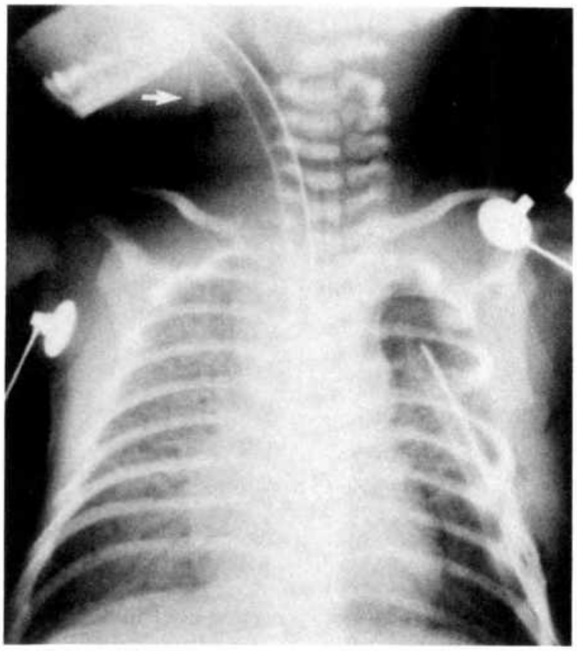

FIG. 1.

Antero-posterior chest radiograph of 3-day-old female with hypoplastic left-heart syndrome showing HOC (arrow).

of the HE in radiographs taken during the first post-natal month was 16.1% in the autopsy control series, with female infants showing increased visibility compared with males (22.2% versus 13.6%). Five infants in this control series were Hispanic (4) or Black (1), and there was no apparent ethnic effect on the data. The incidence of visible HE in radiographs taken in the first post-natal month was increased in infants with IS (5/7 = 71%), or with complete TGV (5/10 = 50%, $p < 0.05$), as compared with 16% for the autopsy control series (see Fig. 3 and Table I), but was only 20% (3/15) in infants with DS with CHD.

The ratio % HOC visible/% HE visible for the autopsy control series was 4.44. The value of this ratio was low for autopsied infants with IS (1.40) and complete TGV (2.00) but was not abnormal (5.00) for the infants with DS with CHD.

DISCUSSION

Tompsett and Donaldson (1951) reported the incidence of a radiographically visible HOC in 500 normal neonates to be 75.2%, with no difference between the sexes. The findings in this report and those of a previous study (Wells et al, 1986) confirm those observations. The previous study showed significantly low incidence of visible HOC in radiographs of infants with DGS, non-DGS TOF, or non-DGS IAA in the first post-natal month. In contrast, all comparable neonates with IS, complete TGV or DS with CHD in this study had 100% radiographic visibility of the HOC (Figs 2 and 3 and Table I). This observation, at least for infants with DS, was an unexpected finding, since delayed ossification of other centres has been reported in this syndrome (Hall, 1966; Willich et al, 1975; Taybi, 1983). Equally unexpected was the finding that the five infants in this study with DS who also had TOF had increased visibility of the HOC (100%) compared with patients with TOF alone (14%) (Wells et al, 1986).

Kuhns et al (1973) have reported the incidence of radiographically visible HE to be 15% at term, with an increased incidence (78%) in neonates with TGV, and Kuhns and Finnstrom (1976) found the incidence at term, in a different population, to be 10%. Because of

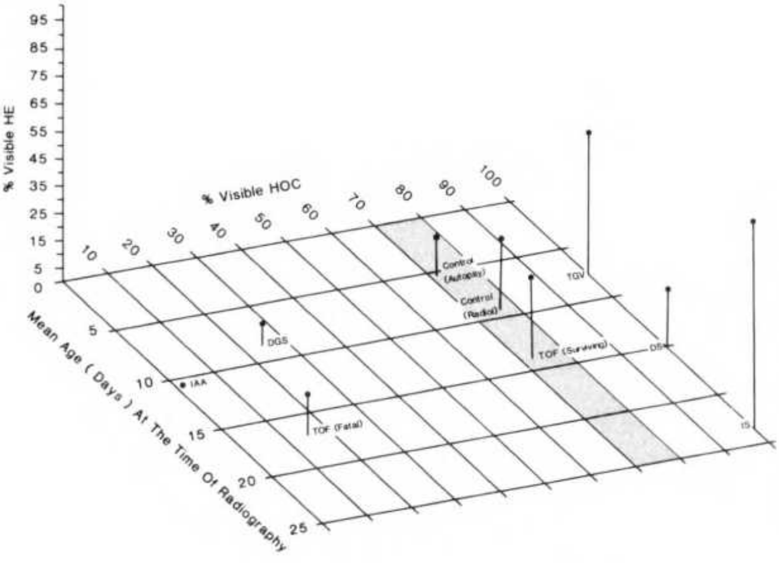

FIG. 2.

Relationship of % radiographically visible HOC and HE to average age of different patient groups at time of radiography, showing three trends compared with normal % visible HOC (shaded band): (1) significantly low % visible HOC in neonates with DGS, non-DGS TOF (fatal) or non-DGS IAA; (2) an increased % visible HOC in neonates with IS, TGV and DS, with (3) those with IS and TGV also showing increased % visible HE.

TABLE I

INCIDENCE OF VISIBILITY OF THE HOC AND OF THE HE IN RADIOGRAPHS TAKEN DURING THE FIRST POST-NATAL MONTH, FOR GROUPS OF INFANTS WITH VARIOUS TYPES OF CHD

Patient group	No. of cases	% visible HOC	χ^2	% visible HE	χ^2	% HOC / % HE	Average age (days) at radiography
Tomsett & Donaldson, 1951		376/500 = 75.2		—		—	
Controls (non-CHD) F = 13, M = 24	37	28/ 37 = 75.7		5/37 = 13.5		5.61	9.15
Controls (autopsy series) F = 9; M = 22	31	22/ 31 = 71.0	NS	5/31 = 16.1	*	4.41	5.1
DS with CHD F = 6; M = 9	15	15/ 15 = 100	*	3/15 = 20.0	*	5.00	15.2
IS F = 2; M = 5	7	7/ 7 = 100	*	5/ 7 = 71.4	<0.05†	1.40	23.2
TGV F = 4; M = 6	10	10/ 10 = 100	*	5/10 = 50.0	< 0.05	2.00	7.6
DGS F = 9; M = 7	16	4/ 16 = 25.0	<0.01†	1/16 = 6.25	*	4.00	8.7
partial, 11		4/ 11 = 36.0	*	—	*	—	
complete, 5		0/ 5 = 0	*	—	*	—	
TOF (non-DGS) F = 9; M = 5 (fatal)	14	2/ 14 = 14.0	<0.01†	2/14 = 14.0	*	1.00	16.8
IAA (non-DGS) F = 2; M = 2 (fatal)	4	0/ 4 = 0	*	0/ 4 = 0	*	—	12.3
TOF (non-DGS) F = 5; M = 6 (not fatal)	11	8/ 11 = 72.7	NS	3/11 = 27.2	*	2.67	13.7
IAA (not fatal)	2	2/ 2 = 100	*	0/ 2 = 0	*	—	18.5
Total	147						

*χ^2 statistic not done because small numbers do not permit valid statistical results.
†Probable significance, compared with autopsy control series or non-CHD controls

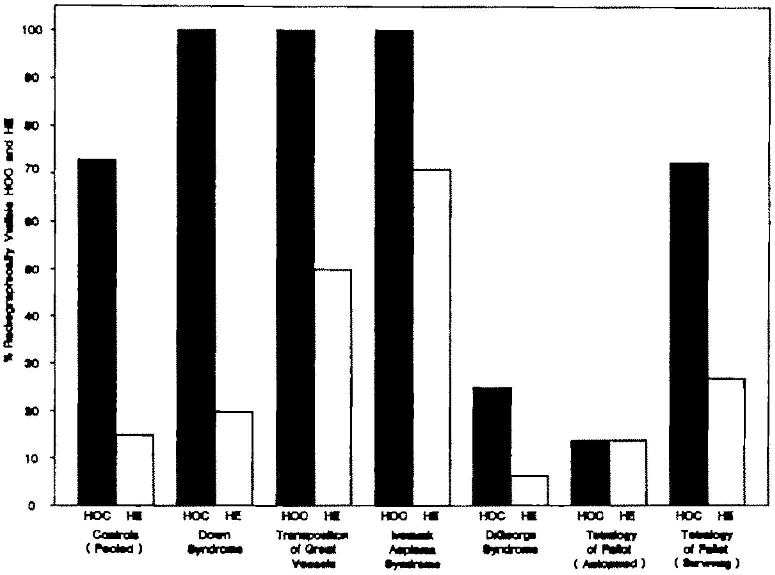

FIG. 3.

Incidence of radiographically visible HOC and HE in the first post-natal month. Neonates with DGS and non-DGS TOF (both groups autopsied) show significantly low % visible HOC compared with the pooled controls or non-DGS TOF (surviving) groups. Neonates with DGS also demonstrate low % visible HE values. Increased % visible HOC is seen in neonates with DS, TGV and IS, increased % visible HE is seen in IS and TGV.

uncertainty about the possible inclusion of patients with IS in the category "transposition of great vessels" in Kuhns' data, in the present study the radiographic incidence of HE in patients with IS and those with TGV was analysed separately (Fig. 2 and Table I), with the finding that neonates with both IS and TGV show an increased incidence of visible HE (71% and 50%, respectively).

Review of the available radiographs of the patients with DGS, non-DGS TOF or non-DGS IAA (Wells et al, 1986) showed an abnormally low incidence of visibility of both the HOC and the HE in infants with DGS or non-DGS IAA, while infants dying with non-DGS TOF showed reduced visibility of the HOC only. Abnormal migration of neural crest cells into the region of developing branchial pouches III and IV, and branchial arch IV, has been proposed as a mechanism of DGS (Taleporos et al, 1978; Brockman & Kirby, 1984; Binder, 1985). The above observations raise the possibility that the migration of neural crest cells may influence the development of the appendicular as well as the axial skeleton.

The varied radiographic findings seen in neonates of: reduced visibility of the HOC and the HE in patients with DGS and in those with non-DGS IAA; of reduced incidence of visibility of the HOC but not of the HE in patients with non-DGS TOF; and increased visibility of HOC in patients with IS, complete TGV or DS with CHD, demonstrate a variety of relations of CHD to skeletal structures. Since the hyoid bone normally begins to ossify in the 20th gestational week (Hill, 1939) while the HE is not normally radiographically visible until about the 37th week of gestation (Kuhns et al, 1973), it is obvious that reduced incidence of visibility of HOC will more commonly be of diagnostic aid than increased visibility (cf. DGS), whereas increased incidence of visibility of the HE will more commonly be useful (cf DS with CHD versus IS). Radiological visibility of an ossification centre depends both on its size and on its degree of maturation. Data of the sort presented in this study may shed light on the stage of maturation of the skeletal system generally in some disorders or on specific deviation of some centres from others in certain conditions, either as a reflection of primary pathogenetic mechanism(s) or as a secondary feature Whether of use simply as a diagnostic aid or as a clue to more fundamental pathogenetic processes, the data of this and the preceding paper (Wells et al, 1986) appear to offer suggestions for future studies.

The material of both these studies does not permit reliable conclusions as to when the HOC becomes radiographically visible in patients with those types of CHD with low incidence of visible HOC in radiographs taken during the first post-natal month—DGS (25%), non-DGS TOF (fatal) (14%), non-DGS IAA (fatal) (0%). In the material of the previous study, none of the 16 patients with DGS nor the four with fatal non-DGS IAA had diagnostic radiographs taken after the age of 1 month. Of the 14 infants with fatal non-DGS TOF, only three had diagnostic radiographs taken after the first month. The HOC was visible in one of these patients at 3 months, but not in the other two at ages 77 days and 1 year, respectively.

Further study would be of use in determining whether, for any of the categories with reduced incidence of visible HOC in radiographs taken during the first month of life, the reduced visibility is due to small size of the HOC anlage (hypoplasia), to retardation of the process of endochondral bone formation (dysmaturity), to reduced formation of bone matrix (osteopenia), or to reduced degree of mineralisation of calcified cartilage matrix or bone matrix (osteomalacia), or whether the HOC never becomes visible and can be presumed to be "absent" in some patients or categories of patients.

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REFERENCES

Binder, M, 1985. The teratogenic effects of a bis (dichloroacetyl) diamine on hamster embryos Aortic arch abnormalities and the pathogenesis of the DiGeorge syndrome *American Journal of Pathology, 118*, 179–193.

Brockman, D E. & Kirby, M. L., 1984. Dependence of thymus development on derivatives of the neural crest *Science, 223*, 498–500

Hall, B., 1966. Mongolism in newborn infants *Clinical Pediatrics, 5*, 4–12.

Hill, A H., 1939. Fetal age assessment by centers of ossification. *American Journal of Physical Anthropology, 24*, 251–272

Kuhns, L. R., Sherman, M. P., Poznanski, A. K. & Holt, J. F., 1973. Humeral-head and coracoid ossification in the newborn. *Radiology, 107*, 145–149.

Kuhns, L. R. & Finnstrom, O., 1976. New standards of ossification of the newborn. *Radiology, 119*, 655–660

Taleporos, P, Salgo, M. P. & Oster, G., 1978. Teratogenic action of a bis (dichloroacetyl) diamine on rats: patterns of malformations produced in high incidence at time limited periods of development. *Teratology, 18*, 5–16.

Taybi, H., 1983 *Radiology of Syndromes and Metabolic Disorders*. (Year Book Medical Publishers, Chicago, London).

Tompsett, A. C. & Donaldson, S. W, 1951. The anterior tubercle of the first cervical vertebra and the hyoid bone. their occurrence in newborn infants *American Journal of Roentgenology, 65*, 582–584.

Wells, T R., Gilsanz, V., Senac, M. O., Landing, B H, Vachon, L & Takahashi, M., 1986. Ossification centre of the hyoid bone in DiGeorge syndrome and tetralogy of Fallot. *British Journal of Radiology, 59*, 1065–1068.

Willich, E., Fuhr, U., Kroll, W., 1975. Skeletal manifestations in Down's syndrome Correlation between roentgenologic and cytogenetic findings. *Annales de Radiologie, 18*, 355–358.

1986, *The British Journal of Radiology*, 59, 1073–1078 NOVEMBER 1986

Value of radionuclide oesophageal transit in studies of functional dysphagia

By J. M. Llamas-Elvira, M. Martinez-Parades,* R. Sopena-Monforte, †V. Garrigues, *C. Cano-Terol and T. Velasco-Lajo

Department of Radiology and Physical Medicine, Faculty of Medicine, Cordoba University, Cordoba, Spain, and *Nuclear Medicine Department and †Digestive Medicine Department, "La Fe" Hospital, Valencia, Spain

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ABSTRACT

Radionuclide oesophageal transit time was evaluated in 70 individuals, divided into three groups: normal individuals, patients with non-organic dysphagia and patients with primary oesophageal motility disorders treated with per-endoscopic forced pneumatic dilatation. In all of them the oesophageal transit time of a bolus of water with 18.5 MBq (500 μCi) of ^{99}Tc^{m} sulphur colloid was assessed, as was the percentage of residual activity of the bolus in the oesophagus. There was a significant difference in these parameters between the control group and the group with non-organic dysphagia, the diagnostic capacity of this test being 93% sensitivity, 100% specificity, 100% positive predictive value and 90% negative predictive value, which suggests its inclusion in diagnostic protocols of dysphagias. In patients with primary oesophageal motility disorders, a significant decrease in values of residual activity has been observed after treatment with per-endoscopic forced pneumatic dilatation.

Since radionuclide oesophageal transit was introduced in 1972 by Kazem, various authors (Gross et al, 1979; Tolin et al, 1979, Russell et al, 1981; Holloway et al, 1983; Kjellen et al, 1984) have evaluated the usefulness of this technique in the diagnosis and assessment of therapy for patients with functional oesophageal pathology and have considered it to be an easy method, comfortable for the patient, exempt from risks and with a high diagnostic reliability in this type of condition. However, its exact place in the diagnostic protocols of patients with dysphagia and in assessing the efficiency of the treatment of primary oesophageal motility disorders has still not been conclusively established.

The purpose of this study is twofold: firstly, to analyse through a prospective study the diagnostic usefulness of radionuclide oesophageal transit time in patients with non-organic dysphagia and, secondly, to assess the usefulness of the technique as an objective method of control of the therapeutic efficiency of pneumatic dilatation in patients with primary oesophageal motility disorders.

PATIENTS

Seventy patients were divided into three groups

Controls

In this group there were 18 individuals (13 male, five female) with no digestive symptoms or any systemic illness, with an age range of 25–42 (mean 34) years. They all volunteered to submit to radionuclide oesophageal transit estimation after being completely informed about the procedure.

Patients with non-organic dysphagia

All the patients at the Digestive Medicine Department of "La Fe" Hospital between January and December 1985 suffering from dysphagia were included in a diagnostic protocol that included video radiology, oesophagoscopy, radionuclide oesophageal transit estimation, manometry and monitoring of pH. Thirty patients were selected in whom the existence of an organic oesophageal lesion had been excluded by endoscopic and video radiological studies. There were 17 males and 13 females, with an age range of 30–81 (mean 58) years.

The patients were classified according to the criteria of Vantrappen et al (1979), taking into account peristalsis (P, present; p, absent), lower oesophageal sphincter relaxation capacity (R, normal relaxation; r, no or incomplete relaxation), and the character of deglutitive response (V, vigorous, *i.e* more than three consecutive waves or waves lasting more than 6 s or with an amplitude higher than 120 mm Hg; v, non-vigorous). Using these parameters two subgroups were defined: achalasia (prv, prV) and intermediate motility disorder (any other combination). Two more possibilities were observed: normal findings and a diagnosis of sympomatic peristalsis (Benjamin et al, 1979). The latter consisted of primary contraction waves which have an average amplitude over 120 mm Hg and attain a maximum amplitude of over 200 mm Hg.

The manometric patterns of the patients in this group are presented in Table I.

Patients with primary oesophageal motility disorders treated with per-endoscopic pneumatic dilatation

All patients diagnosed with a primary oesophageal motility disorder suitable for non-pharmacological treatment were offered the possibility of being treated with per-endoscopic forced pneumatic dilatation. Of the

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Address for correspondence: J M Llamas-Elvira, Departamento de Radiologia y Fisioterapia, Facultad de Medicina, Avda Menendez Pidal s/n, 14004 Cordoba, Spain

TABLE I

MANOMETRIC PATTERN, PERCENTAGE OF RESIDUAL ACTIVITY AND TRANSIT TIME IN PATIENTS OF THE SECOND GROUP

Manometric pattern	Standing		Supine	
	Residual activity (%)	Transit time (s)	Residual activity (%)	Transit time (s)
prv	85	> 45		
prv	70	> 45		
prv	67	> 45		
prv	78	> 45		
prv	75	> 45		
prv	82	> 45		
prv	72	> 45		
prv	79	> 45		
prv	16	> 45		
pRv	64	> 45		
pRv	69	> 45		
pRv	66	> 45		
pRv	75	> 45		
pRv	77	> 45		
pRV	75	> 45		
pRV	79	> 45		
pRV	25	> 45		
PRv	32	> 45		
Prv	6	7	45	> 45
SP	8	7	43	> 45
SP	19	> 45		
SP	18	> 45		
SP	3	17	60	> 45
SP	6	5	8	9
SP	5	4	7	8.5
NM	15	> 45		
NM	6.5	19		
NM	15	> 45		
NM	19	> 45		
NM	16	> 45		

P = peristalsis present, p = peristalsis absent, R = normal relaxation, r = no or incomplete relaxation, V = vigorous deglutitive response, v = non-vigorous deglutitive response, SP = symptomatic peristalsis and NM = normal manometry

22 patients selected for this treatment, a radionuclide oesophageal transit was carried out 1 month before and after the dilatation on seven (four with achalasia and three with intermediate motility disorder) Four of these were males and three females, with an age range of 30–75 (mean 45) years. In another 15 patients, 13 with achalasia and two with intermediate motility disorder, radionuclide oesophageal transit estimation was carried out only after dilatation (mean 9 months, range 6–12 months). There were eight males and five females, with an age range of 37–77 (mean 58) years.

Before dilatation, all patients were in Clinical Stage IV, according to a previously established scale (Table II). After dilatation, during the radionuclide study, three patients were in Clinical Stage IV, three in Stage III, six in Stage II and 10 in Stage I.

TABLE II

CLINICAL CLASSIFICATION OF PATIENTS WITH PRIMARY OESOPHAGEAL MOTILITY DISORDERS

Stage	Symptoms
I	None
II	Dysphagia or pain (lasting less than 2 min. Frequency once a week or less)
III	Dysphagia or pain (lasting 2–10 min. Frequency: more than once a week, less than once a day)
IV	Dysphagia or pain (lasting more than 10 min. Frequency: once a day or more). Weight loss and/or regurgitation

METHODS

Videoradiology

A barium swallow was performed and recorded on videotape. All studies were later carefully analysed by a radiologist who reported on the normality or abnormality of the examination, and, in abnormal cases, about the organic or functional nature of the process.

Oesophagoscopy

Endoscopic examinations were performed with a forward viewing endoscope. The endoscopist was asked to exclude the possibility of organic oesophageal disease. In all cases, tissue samples of the oesophagogastric junction were taken for histopathological study.

Radionuclide oesophageal transit estimation

All studies were performed in the morning after an overnight fast of at least 8 h. The individual was examined in a standing and/or supine position, in front of or under a digital gamma camera (Toshiba, GCA-501 S) with a low-energy general-purpose collimator (RDC 43 A). Through a straw, the patient sucked 15 ml of water with 18.5 MBq (500 μCi) of ^{99}Tc^{m} sulphur colloid, kept in the mouth and swallowed, on request, in one deglutition. Images were then taken every 0.5 s for 45 s, on a 64 × 64 matrix, the patient having been asked not to swallow during this period

An area of interest of the oesophagus was then selected on the computer screen after identifying its proximal and distal ends (during the study an external marker was placed at the level of the cricoid cartilage). This area was divided in three equal parts: the upper, middle and lower thirds of the oesophagus (Fig. 1). Later, the computer generated time–activity curves of the oesophageal area and of each one of its thirds.

In most cases, the values towards the end of the curve fluctuated, and, in order to facilitate subsequent calculations, a straight line was drawn at the arithmetic mean of the values of the last 20 points, corresponding to the last 10 s.

The curves were analysed quantitatively and qualitatively. For the quantitative analysis, two parameters were used: the percentage of residual activity (residual activity divided by maximal activity, expressed as a

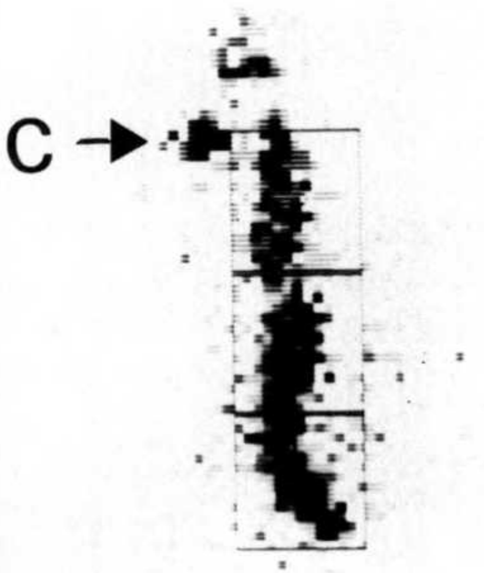

FIG. 1.

Scintigraphic image of the oesophagus divided into three equal parts, the upper, middle and lower thirds. C: external marker placed on the cricoid cartilage.

percentage), and the transit time (seconds elapsed from the arrival of the bolus until the activity equalled the percentage of normal residual activity obtained by the control group) (Fig. 2). These values were calculated for the whole of the oesophagus and for each one of the thirds into which it had been divided. Qualitatively, two phenomena were taken into account: sequentiality, assessed by the sudden upstroke of the activity peak in each oesophageal third, and retention profile, when it was abnormal, classifying it as adynamic or static when it was relatively stable, and dynamic when it presented large transitory fluctuations that suggested bidirectional transit of the radionuclide.

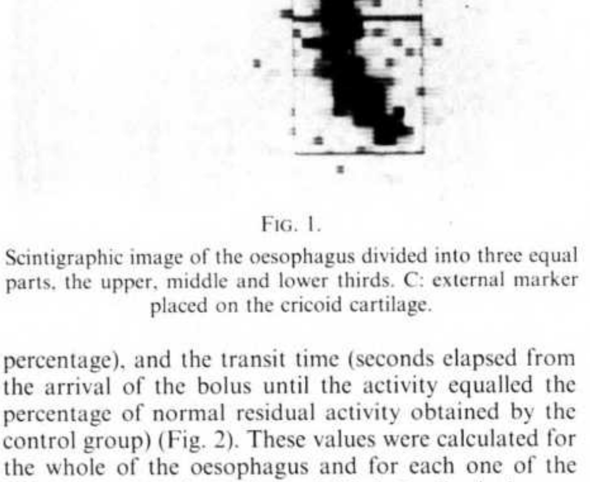

FIG. 2.

An ideal time–activity curve, showing how residual activity (R) and transit time (TT) have been calculated.

Oesophageal manometry and pH measurement

Manometric studies were performed following a method described previously (Ponce et al, 1982) with a low distensibility pneumohydraulic pump (Arndorfer, Medical Specialities, Wisconsin) that perfused the three catheters to the exploratory probe.

Gastro-oesophageal reflux was excluded in all patients after a standard pH measurement, following a method described previously (Ponce et al, 1982).

STATISTICAL CALCULATIONS

Statistical assessment was carried out using Student's t-test for paired or unpaired data (whichever they were), considering the differences as statistically significant for $p < 0.05$. Values in the text are expressed as arithmetic mean ± 1 SD. The values of the diagnostic sensitivity were obtained with the formula $TP/(TP+FN)$, the values of diagnostic specificity with $TP/(TP+FP)$, and the predictive values of the negative result with $TN/(TN+FN)$, where TP = true positive, FN = false negative, TN = true negative, and FP = false positive.

RESULTS

Controls

In the control group, with normal individuals, the mean values of the percentage of residual activity were 7.3 ± 1.9% in all studies of standing patients and 8.8 ± 1.6% for patients in a supine position. In all cases, it was less than 10% in the standing position and less than 15% in the supine; these values were accepted as the limits of normality.

The mean transit time in the standing position was 3.3 ± 0.3 s for the upper third, 4.66 ± 0.70 s for the middle third and 5.7 ± 1.2 s for the lower third and 5.9 ± 1.1 s for the whole of the oesophagus. In supine position, the mean transit time was 3.9 ± 0.7 s, 4.9 ± 1.6 s, and 6.2 ± 1.4 s for the upper, middle and lower oesophagus, respectively, and 7.8 ± 1.6 s for the whole of the oesophagus. In all cases and in either position, the total transit time was less than 10 s, which was accepted as the upper limit of normality. Both the percentage of residual activity and transit time were significantly lower in the standing than in the supine position ($p < 0.01$ and $p < 0.005$, respectively).

All individuals in this group displayed sequentiality in activity peaks (Fig. 3).

Patients with non-organic dysphagia

The videoradiographic study of this group detected abnormality in the nine patients with achalasia (100% sensitivity). Out of the 10 patients with intermediate motility disorder, only six were considered abnormal (68% sensitivity). Three of the six patients with symptomatic peristalsis (50% sensitivity) and none of the five patients with normal manometry (0% sensitivity) presented abnormalities.

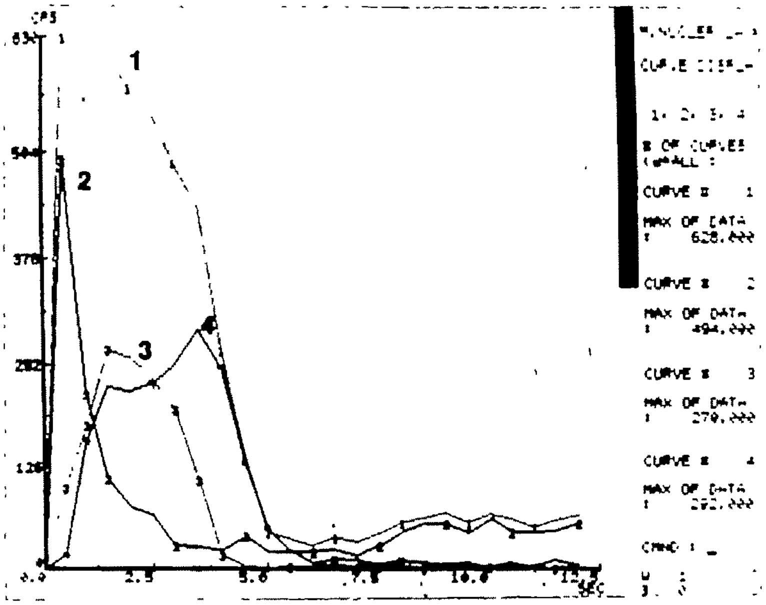

FIG. 3.

Time–activity curves from a normal individual for the whole oesophagus (1) and each one of its thirds: upper (2), middle (3) and lower (4). Note sequential activity peaks in the oesophageal thirds. The graph stops at 12.5 s.

The time–activity curves generated in patients with achalasia and intermediate motility disorder presented a pattern of adynamic retention of the radionuclide, mainly due to stasis in the lower third and, to a lesser extent, the middle third, whereas activity in the upper third was normal (Fig. 4). A dynamic retention pattern was observed in one of the three patients with intermediate motility disorder and vigorous motility pattern (Fig 5). In one patient with intermediate motility disorder who had not lost the capacity to generate primary contractions and in four patients with symptomatic peristalsis, the curves presented a sequential profile (Fig. 6).

Table I presents the values of the percentage of residual activity and transit time in the standing and supine positions of patients in this group. Only two of the patients with symptomatic peristalsis had all normal values. Therefore, the analysis of the diagnostic capacity of radionuclide oesophageal transit gave the following results: 93% sensitivity, 100% specificity, 100% positive predictive value and 90% negative predictive value.

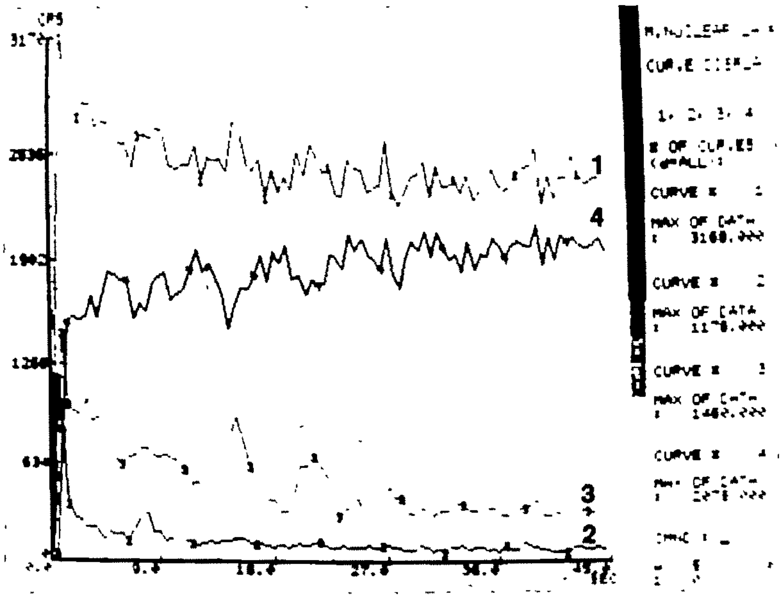

FIG 4.

Time–activity curves in patient with achalasia, for the whole oesophagus (1) and the upper third (2), middle third (3) and lower third (4). Note adynamic retention of the radionuclide, mainly in the lower third

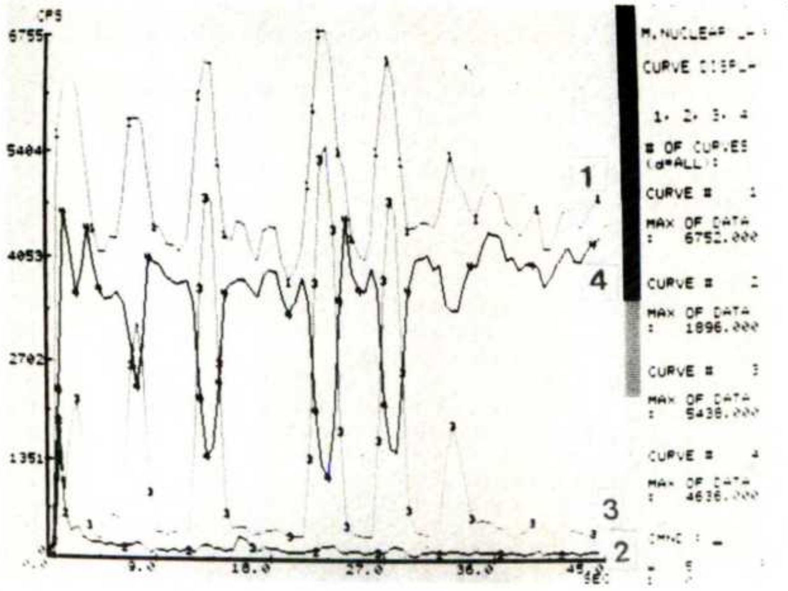

FIG. 5.

Time–activity curves from a patient with vigorous motility disorder for the whole oesophagus (1) and each one of its thirds: upper (2), middle (3) and lower (4). Note dynamic retention pattern with activity interchange between the middle and lower thirds.

Patients with primary oesophageal motility disorders treated with penumatic dilatation

In the seven patients with pre- and post-dilatation radionuclide studies, the percentage of residual activity changed from 75.2±7.2% to 47.3±6.1% ($p < 0.05$), but no case reached normal levels. The decrease was greater in the patients who, after dilatation, were in Clinical Stage I.

The percentage of residual activity in the 15 patients with post-dilatation radionuclide oesophageal transit was 32.2±25.1%, significantly lower than the percentage of residual activity obtained by untreated patients with similar pathology (non-organic dysphagia). In four patients in Clinical Stages I, II and IV, the percentage of residual activity did not reach normal levels.

DISCUSSION

In our study, transit time obtained in normal subjects (always under 10 s) was comparable with that obtained in previous reports (Kazem, 1972; Bosch et al, 1977; Tolin et al, 1979; Russell et al, 1981; Benjamin et al, 1983). Transit time and the percentage of residual activity in the standing position were significantly lower than in the supine. This may be attributed to the fact that the force of gravity is added to the propulsive force

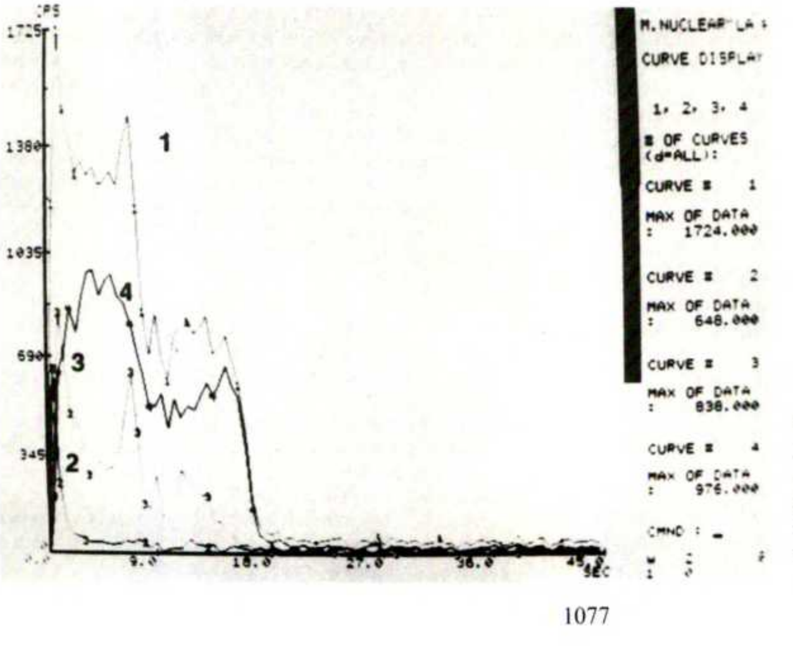

FIG. 6.

Time–activity curves in patient with symptomatic peristalsis, for the whole oesophagus (1) and each one of its thirds: upper (2), middle (3) and lower (4). Note sequentiality in the activity peaks and also increased transit time (18 s) with normal percentage of residual activity.

of the pharyngeal and oesophageal contraction. Kaye and Wexler (1981) have shown changes in amplitude and propagation speed of oesophageal contraction waves depending on whether the subject was examined in the standing or the supine position, especially after swallowing liquids

In the light of our results and of those of Russell et al (1981), it seems evident that there is a progressive increase in transit time in the different thirds of the oesophagus and a sequential movement of activity peaks in these thirds. This is confirmed by the fact that this sequential pattern was absent in patients with achalasia and in patients with intermediate motility disorders with simultaneous oesophageal contraction. On the other hand, it was present in four of the patients with symptomatic peristalsis who, by definition, remained with peristalsis, and in the only patient with intermediate motility disorder who had peristaltic oesophageal contraction. Richter et al (1983), when performing combined studies of manometry and radionuclide oesophageal transit, indicated that the mere presence or absence of peristalsis, and not the amplitude, length or repetitiveness of the waves, would have an effect on the rate of oesophageal transit. This very fact would explain why the highest transit time is obtained in patients with achalasia (Tolin et al, 1979; Holloway et al, 1983) and with intermediate motility disorder, while patients with symptomatic peristalsis and other motility alterations with unaffected peristalsis have a less altered transit time (Benjamin et al, 1983; Richter et al, 1983). The dynamic retention pattern observed in a patient with vigorous oesophageal contraction would reflect the bidirectional transit of the radionuclide.

In our study, sensitivity of radionuclide oesophageal transit was higher than that of videoradiology, except in patients with achalasia, who afforded identical sensitivity. Radionuclide studies are unable, however, to differentiate clearly functional from organic obstructions (Kazem, 1972), so they cannot be considered as substitutes for radiology or endoscopy. The good diagnostic rates obtained by radionuclide oesophageal transit allow us to suggest their inclusion in diagnostic protocols of patients with dysphagia. After excluding the presence of organic lesion, by endoscopy and/or radiography, one would lead on to radionuclide oesophageal transit. If it were abnormal, a manometric study could be carried out to determine the type of motility disorder. If, on the other hand, it were normal, the study would have ended, thus avoiding manometric studies in some patients.

In previous publications (Russell et al, 1981; Kjellen et al, 1984), radionuclide oesophageal transit has proved to be a useful technique for studying patients with dysphagia and normal manometry, producing the only objective information about anomalous oesophageal function. Similar results were obtained in our five patients with these characteristics. Serial prospective studies of the evolution of these patients would tell us whether or not they are exhibiting the initial stages of an oesophageal motility disorder.

Control of the different therapeutic criteria in patients with primary oesophageal motility disorder is mainly clinical, although it may be supported by objective studies whose results do not always coincide with the clinical impressions. In our studies a significant reduction of the percentage of residual activity was found after pneumatic dilatation, although it only occasionally reached normal limits, coinciding with similar results in other publications (Gross et al, 1979, Holloway et al, 1983). However, these tests may well prove unnecessary in view of the positive clinical assessment

REFERENCES

BENJAMIN, S. B., GERHARDT, D. C. & CASTELL, D. O., 1979 High amplitude, peristaltic esophageal contractions associated with chest pain and/or dysphagia. *Gastroenterology, 77,* 478–483

BENJAMIN, S B., O'DONNELL, J. K , HANCOCK, J , NIELSEN, P & CASTELL, D O , 1983. Prolonged radionuclide transit in "nutcracker esophagus" *Digestive Diseases and Sciences, 28,* 775–779.

BOSCH, A., DIETRICH, R., LANARO, A. E & FRIAS, Z., 1977 Modified scintigraphic technique for the dynamic study of the esophagus *International Journal of Nuclear Medicine and Biology, 4,* 195–199.

GROSS, R., JOHNSON, L F. & KAMINSKI, R J , 1979 Esophageal emptying in achalasia quantitated by a radioisotope technique. *Digestive Diseases and Sciences, 24,* 945–949

HOLLOWAY, R. H , KROSIN, G., LANGE, R. C , BAUE, A E & MCCALLUM, R. W , 1983. Radionuclide esophageal emptying of a solid meal to quantitate results of therapy in achalasia *Gastroenterology, 84,* 771–776.

KAYE, M. D & WEXLER, R. M , 1981. Alteration of esophageal peristalsis by body position *Digestive Diseases and Sciences, 26,* 897–901.

KAZEM, I., 1972. A new scintigraphic technique for the study of the esophagus *American Journal of Roentgenology, 115,* 681–688

KJELLEN, G., SVEDBERG, J B & TIBBLING, L., 1984. Solid bolus transit by esophageal scintigraphy in patients with dysphagia and normal manometry and radiography. *Digestive Diseases and Sciences, 29,* 1–5.

PONCE, J , JUAN, M., MIRALBES, M , MIR, J & BERENGUER, J., 1982 Esofago en cascanueces (anomalía motora caracterizada por contracciones esofa'gicas peristalticas de alta amplitud) *Gastroenterología y Hepatología, 5,* 541–545.

RICHTER, J. E., BLACKWELL, J N , WU, W C , COWAN, R J , JOHNS, D. N & CASTELL, D O., 1983. Assessment of liquid bolus transit (LBT) by simultaneous radionuclide transit and esophageal manometry. *Gastroenterology, 84,* 1285–1289

RUSSELL, C. O. H , HILL, L D., HOLMES III, E R , HULL, D A , GANNON, R & POPE II, C. E , 1981 Radionuclide transit: a sensitive screening test for esophageal dysfunction. *Gastroenterology, 80,* 887–892.

TOLIN, R. D., MALMUD, L S , REILLEY, J & FISHER, R S., 1979. Esophageal scintigraphy to quantitate esophageal transit (quantitation of esophageal transit). *Gastroenterology, 76,* 1402–1408.

VANTRAPPEN, G., JANSSENS, J., HELLEMANS, J & COREMANS, G., 1979. Achalasia, diffuse esophageal spasm, and related motility disorders. *Gastroenterology, 76,* 450–457

1986, *The British Journal of Radiology*, *59*, 1079–1082 NOVEMBER 1986

Intraperitoneal toxicity of Hytrast: an experimental study

By A. Z. Ginai, *F. J. W. Ten Kate, †R. G. M. Ten Berg and K. Hoornstra

Departments of Radiology and *Pathology, University Hospital Dijkzigt, Rotterdam, The Netherlands

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ABSTRACT

The toxic effects of Hytrast were studied on the peritoneum of laboratory rats in order to define the lethal dose and possible causes of toxicity. The results show that Hytrast, due to its toxicity, should not be used in any clinical situation where gastrointestinal tract perforation or leakage is a possibility

During the course of recent experimental work, carried out to find the most suitable contrast medium for use in the gastrointestinal tract in cases where leakage outside the gastrointestinal tract could be suspected (Ginai et al, 1984, 1985; Ginai, 1985), we became aware of the toxic effects of Hytrast when injected into the peritoneum of rats. In our previous experimental study on the peritoneum (Ginai, 1985), all animals received 1.5 ml of one of the contrast media—Micropaque (Nicholas), pure barium sulphate, Dionosil (Glaxo), Hytrast (Guerbet), Gastrografin (Schering), Amipaque (Nyegaard) or Hexabrix (May & Baker)—intraperitoneally. It was planned to sacrifice the animals at intervals of 1 day, 2 days, 4 days, 8 days or 42 days after injection of contrast medium, but the Hytrast group reacted exceptionally badly in that all the animals died after about 48 h (Ginai, 1985). It is the purpose of this study to evaluate the toxic effects of Hytrast in the peritoneum of laboratory rats.

MATERIAL AND METHOD

Twenty male rats (Wistar strain, outbred stock, WU/Cpb) (Zeist) weighing between 264 g and 295 g were used. The rats were divided into five groups of four rats each. Four of the groups received Hytrast (aqueous suspension of N-(propyl-2 : 3-diol)-3 : 5 diiodo-4-pyridone (NPP) and 3 : 5 diiodo-4-pyridone (DIP)) and Group 5 acted as a control (see below).

Group 1	1.5 ml	Hytrast
Group 2	0.75 ml	Hytrast
Group 3	0.375 ml	Hytrast
Group 4	0 19 ml	Hytrast
Group 5	1 5 ml	physiological saline

The rats were anaesthetised by ether inhalation. Hytrast or physiological saline was injected into the peritoneal cavity with a blunt polyethylene catheter via a small midline abdominal incision. The incision was then closed with a surgical clip.

Frontal and lateral radiographs of the abdomen and thorax were taken immediately after injection of contrast medium and once again when any animal died or, otherwise, at sacrifice on the 42nd day. The following tissue biopsies were included at dissection:

(1) abdominal wall with the peritoneal lining,
(2) diaphragm (both right and left side),
(3) liver,
(4) spleen,
(5) pancreas,
(6) kidney,
(7) greater omentum,
(8) mesentery,
(9) lymph nodes (thoracic and abdominal when possible),
(10) small bowel (at least two regions), and
(11) large bowel (at least two regions).

All the tissues removed were fixed in 10% buffered formalin for about 2 weeks before histological sections were prepared and stained with haematoxylin and azophloxin. The following grading system was used for the severity of histological reaction:

+ + +	severe reaction,
+ +	moderate reaction,
+	mild reaction,
±	minimal reaction;
–	no reaction.

RESULTS

All four animals in Group 1 (receiving 1.5 ml Hytrast) and two out of four animals in Group 2 (receiving 0.75 ml Hytrast) died. The four animals in Group 1 died within 48 h of administration of Hytrast. The two non-survivors in Group 2 died at 50 h and on the 10th day after injection of contrast medium. All the other animals survived and were sacrificed on the 42nd day.

The animals who died had appeared ill, their food and drink intake was only minimal and they had lost weight. The dissections on these animals were often carried out a few hours, sometimes up to 12 h, after their death. The animals who survived and were sacrificed on the 42nd day had put on a considerable amount of weight (about 200 g) and appeared generally well throughout the experimental procedure.

RADIOLOGICAL APPEARANCES

Group 1 (receiving 1 5 ml Hytrast) showed Hytrast spread around the intestines on the frontal and lateral radiographs taken immediately after intraperitoneal

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Address for correspondence and reprints Dr A. Z. Ginai, Department of Radiology, University Hospital Dijkzigt, Dr Molewaterplein 40, 3015 GD Rotterdam, The Netherlands.

†Present address: Laboratory of Experimental Surgery, Antoni van Leeuwenhoek Ziekenhuis, Cancer Institute of the Netherlands, Amsterdam, The Netherlands.

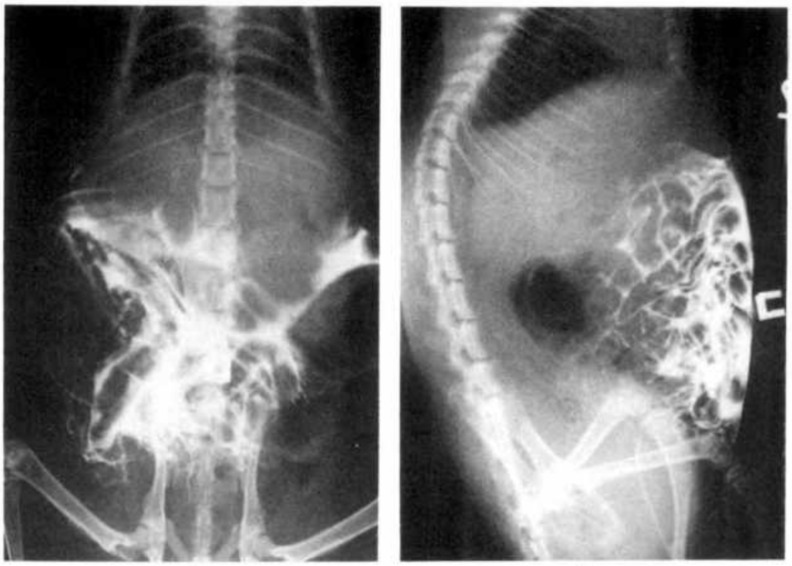

FIG. 1.

(A) Frontal and (B) lateral radiographs showing Hytrast (1.5 ml) in the abdomen of a rat immediately after injection.

injection of contrast medium (Fig. 1). The radiographs of abdomen and thorax taken at about 48 h after contrast medium injection or after the death of these animals showed contrast medium to be flocculated and collected centrally and ventrally in the abdomen, and the bowel appeared denser, with contrast speckles (Fig. 2). The diaphragmatic lymphatic plexus, retrosternal lymph vessels and retrosternal superior mediastinal lymph nodes are seen to be filled with contrast medium on the radiographs (Fig. 2).

Group 2 (receiving 0.75 ml Hytrast). The quantity of Hytrast in the peritoneal cavity was, naturally, less than (half) that in Group 1. Two animals died with similar appearances as Group 1. The two animals who survived were radiographed at 42 days, just before sacrifice, and this showed small contrast rests in the abdomen.

Group 3 (receiving 0.375 ml Hytrast) and *Group 4* (receiving 0.19 ml Hytrast). These groups had similar appearances on radiographs taken immediately after contrast medium injection, with the contrast medium spread around the intestines. The quantity of contrast medium in Group 3, as expected, appeared less than that in Group 2 and the quantity of contrast medium in Group 4 was less than that in Group 3.

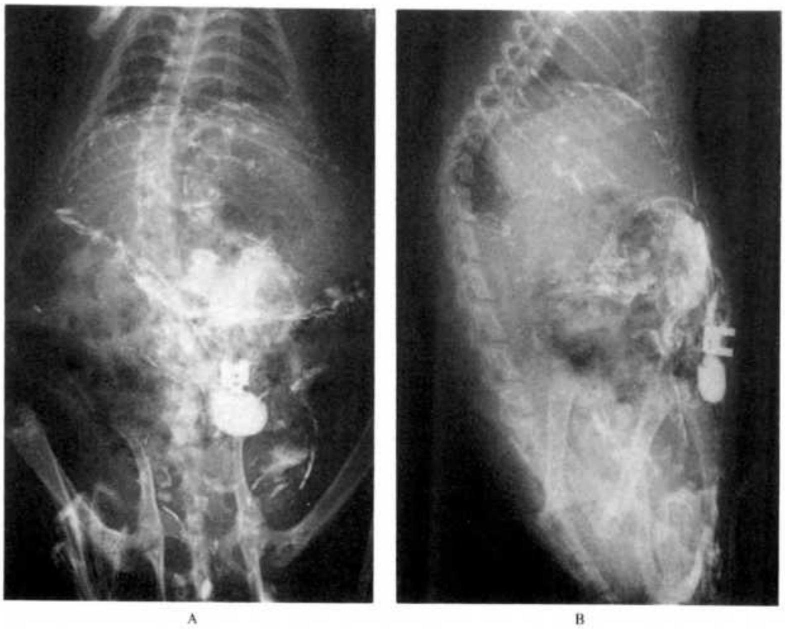

FIG. 2.

Same rat as Fig. 1, 48 h after death. (A) Frontal and (B) lateral radiographs, showing flocculation of contrast medium and its collection more centrally and ventrally in the abdomen. Filling of the diaphragmatic and retrosternal lymphatics and mediastinal lymph nodes with contrast medium is visible.

On the 42-day radiographs, minimal contrast rests were seen in the abdomen. There was no contrast medium seen filling the diaphragmatic lymphatics, retrosternal lymph vessels or lymph nodes.

Group 5 (receiving 1.5 ml physiological saline). This control group showed no abnormalities on the radiographs taken immediately after injection of contrast medium or 42 days after injection.

PATHOLOGICAL OBSERVATIONS

Gross appearances

Group 1. All four animals died about 48 h after injection. Dissection was often carried out several hours after death. A small amount of yellowish or reddish ascitic fluid was found in the abdomen. The contrast medium was seen as whitish plaques on the surface of the omentum, mesentery and abdominal wall and sometimes over the liver. The abdominal surface of the diaphragm showed filling of lymphatic plexuses on both sides. Contrast medium was also seen in the retrosternal lymphatics and lymph nodes.

Group 2. Two animals in this group died, one at 50 h and the other on the 10th day after injection. Slight ascites was seen in one and contrast medium was visible in the abdomen, though less than in Group 1. In the other rat, dying on the 10th day, practically no ascitic fluid was noted. Contrast medium was seen in the mediastinal lymph nodes in both of these rats. The remaining two rats were sacrificed on the 42nd day and showed only tiny contrast rests and some adhesions between the anterior abdominal wall and the small intestine. No ascites was noted. No filling of diaphragmatic lymphatics or retrosternal lymph vessels or lymph nodes was seen.

Groups 3 and 4. These animals were sacrificed on the 42nd day and showed tiny contrast rests anteriorly, usually with some adhesions between the anterior abdominal wall and mesentery or small intestines. No ascites was seen. No filling of lymphatics in the diaphragm or retrosternal region was seen. Mediastinal lymph nodes were not filled with contrast medium.

Group 5. This control group showed no abnormalities on dissection at 42 days.

Histological appearances

Group 1. The abdominal wall and diaphragm showed extensive, acute inflammatory reaction with lymphocytic and histiocytic infiltration and deposits of contrast medium in some places. Necrotic areas were seen on the surface with extensive fibrinous exudate. Similar reaction could be seen in the capsule of the liver. The liver parenchyma was normal. The kidney showed no abnormality. The spleen showed decrease of lymphocytes in the parenchyma. The omentum and peripancreatic fatty tissue showed deposits of contrast medium with a surrounding inflammatory infiltrate (Fig. 3). Contrast medium could sometimes be seen in the mesentery adjacent to the bowel. Transmural segmental necrosis was seen in the large and small bowels and there were also some areas of superficial mucosal and submucosal necrosis. Contrast medium was not visible in the mucosal, submucosal or muscular layers of the bowel. The mediastinal lymph nodes showed necrotising lymphadenitis.

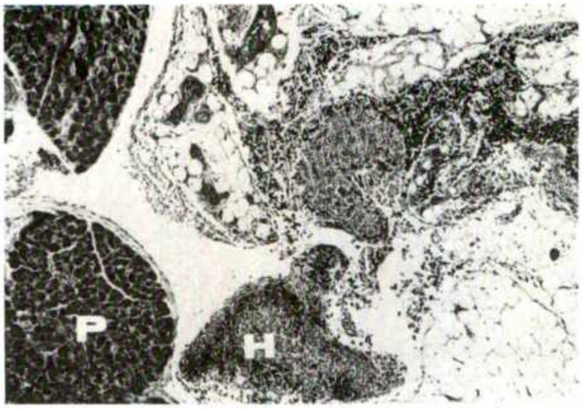

FIG. 3.

Histological section showing Hytrast (H) deposits with inflammatory reaction in the peripancreatic fat (P). Haematoxylin and azophloxin, ×40.

Group 2. The two animals who died showed deposition of contrast medium and inflammatory reaction with histiocytic infiltration in the abdominal wall, diaphragm, omentum and mesentery. Areas of necrosis were also seen in the peripancreatic fatty tissue. In the lymph nodes a sinus histiocytosis was noted. The small and large bowels showed some areas of necrosis.

The two survivors showed no specific abnormalities except small contrast medium deposits in the omentum, with minimal areas of inflammatory cell infiltration.

Group 3. Small deposits of contrast medium were seen in the omentum and mesentery. Some small areas of necrosis were seen in the mucosa of the small bowel and focally in the muscle layer in one of the animals.

Group 4. Fibrosing, chronic inflammatory reaction was seen in the abdominal-wall muscles in one of the animals (probably the site of abdominal incision). Tiny rests of contrast medium were seen in the mesentery and around the liver capsule. In one instance chronic inflammatory reaction was seen in the pancreatic tissue. The bowel showed no abnormality.

Group 5. This control group showed minimal inflammatory infiltrate in the peripancreatic fatty tissue. In one animal, the small bowel showed partial necrosis in places in the superficial layers of mucosa and submucosa.

Table I summarises the tissue reaction with various doses of Hytrast in the peritoneum of rats.

DISCUSSION

The most severe tissue reactions were seen in Group 1 (receiving 1.5 ml Hytrast), in which all the animals died.

TABLE I

HISTOLOGICAL REACTION IN THE PERITONEAL TISSUES OF 16 RATS RECEIVING HYTRAST AND CONTROLS

Animals	Group 1 (1.5 ml Hytrast)	Group 2 (0.75 ml Hytrast)	Group 3 (0.375 ml Hytrast)	Group 4 (0.19 ml Hytrast)	Group 5 (1.5 ml physiological saline)
1	+ + +°	+ +°	+	+	±
2	+ + +°	+ +°	+	+	±
3	+ + +°	+	±	±	±
4	+ + +°	+	±	±	–

°Animals who died; + + + severe reaction; + + moderate reaction; + mild reaction; ± minimal reaction; – no reaction.

Two of the animals in Group 2 (receiving 0.75 ml Hytrast) also died, and these showed moderately severe reaction. All the other animals (10 with Hytrast and four controls) survived and were in good condition when sacrificed on the 42nd day. These animals showed mild to minimal or no tissue reaction (Table 1).

It would, therefore, appear from this study that 1.5 ml of Hytrast intraperitoneally is an absolutely lethal dose for rats weighing about 280 g and that half the dose (0.75 ml of Hytrast) intraperitoneally caused half the animals to die. Further reduction of the Hytrast dose, to a quarter (0.375 ml) and an eighth (0.19 ml) of the original dosage, lead to no deaths.

The full dose of Hytrast used in rats, *i.e.* 1.5 ml, is equivalent to about 375 ml in a 70 kg man, an amount of contrast medium which could possibly enter the peritoneum in a clinical situation of bowel perforation.

From the general clinical, gross pathological and histological appearances seen in the animals who died, the most likely cause of death appears to be a severe exudative, necrotising peritonitis in all tissues of the peritoneum with which Hytrast comes in contact. The liver parenchyma, pancreas and kidney showed no abnormalities. The spleen showed a decrease in lymphocytes. The lymph nodes showed deposition of contrast medium in Group 1 and half of the rats in Group 2, with some necrosis and sinus histiocytosis. This was also noted in the previous experimental work with various contrast media in the peritoneum (Ginai, 1985) and does not appear to be directly related to the death of these animals.

The intestines showed partial or complete intramural necrosis in places. These appearances could suggest ischaemic changes possibly resulting from shock arising from acute peritonitis. It is, however, not possible to confirm this hypothesis or to define any direct relationship between bowel necrosis and death of the animals, as some necrosis was also seen in the animals who survived and even in the control group. Some autolysis or technical factors may also have played a role in these appearances of the bowel.

Hytrast was introduced as a bronchographic contrast medium in 1962. It is a neutral suspension of crystals of N-(propyl-2 : 3-diol)-3 : 5 diiodo-4-pyridone and 3 : 5 diiodo-4-pyridone in a hypertonic aqueous solution of sodium carboxymethyl cellulose (Morley, 1969). The viscosity varies from 6 poises (French preparation) to 2–4 poises (American preparation) at 37°C depending on the quantity of methyl cellulose used in its preparation (Grainger et al, 1970). Hytrast can produce excellent-quality bronchograms but is known to have caused significant reactions in the lungs both in humans and in animals (Greenberg, 1964; Ginai et al, 1984).

Thirty-eight cases of severe reactions following bronchography with Hytrast (including one death) were reported by Agee and Shires (1965). Hytrast also produced the severest reaction in the mediastinum compared with all other contrast media used in the experimental work done on the mediastinum of rats (Ginai et al, 1985). Considering the severe toxicity of Hytrast in the peritoneum (Ginai, 1985) of rats and the very severe toxic reactions in the mediastinum, lungs and pleura of rats (Ginai et al, 1984, 1985; Ginai, 1986), this contrast medium should not be used in the gastrointestinal tract in cases where leakage in any of the above-mentioned regions is a possibility, for example, in post-operative patients with gastrointestinal-tract anastomosis or any other cases where gastrointestinal-tract perforation is suspected.

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REFERENCES

AGEE, O. F. & SHIRES, D. L., 1965. Death after bronchography with a water soluble iodine containing medium. *Journal of the American Medical Association, 194,* 459–461.

GINAI, A. Z., 1985. Experimental evaluation of various available contrast agents for use in the gastrointestinal tract in case of suspected leakage. Effects on peritoneum. *British Journal of Radiology, 58,* 969–978.

——1986. Experimental evaluation of various available contrast agents for use in the gastrointestinal tract in case of suspected leakage. Effects on pleura. *British Journal of Radiology, 59,* 887–894.

GINAI, A. Z., TEN KATE, F. J. W., TEN BERG, R. G. M. & HOORNSTRA, K., 1984. Experimental evaluation of various available contrast agents for use in the upper gastrointestinal tract in case of suspected leakage. Effects on lungs. *British Journal of Radiology, 57,* 895–901.

——1985. Experimental evaluation of various available contrast agents for use in the upper gastrointestinal tract in case of suspected leakage. Effects on mediastinum. *British Journal of Radiology, 58,* 585–592.

GRAINGER, R. G., CASTELLINO, R. A., LEWIN, K. & STEINER, R. N., 1970. Hytrast: experimental bronchography. Comparing two different formulations. *Clinical Radiology, 21,* 390–395.

GREENBERG, D. S., 1964. Pulmonary tissue reaction following Hytrast bronchograms. *Transactions of the American Bronchoesophageal Association, 44,* 106–119.

MORLEY, A. R., 1969. Pulmonary reaction to Hytrast. *Thorax, 24,* 353–358.

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Contrast-enhanced computed tomography of the normal and abnormal gallbladder

By *R. W. Whitehouse, B.Sc., M.B., Ch.B. and D. F. Martin, M.R.C.P., F.R.C.R.

Department of Diagnostic Radiology, The Medical School, Stopford Building, University of Manchester, Oxford Road, Manchester M13 9PT

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ABSTRACT

One hundred and fourteen upper abdominal computed tomography examinations performed before and after intravenous contrast were reviewed. In 48 patients who had no evidence of biliary or pancreatic disease, the mean gallbladder wall attenuation before contrast was 25±13 HU and after contrast 42±18 HU, with a wall thickness of 1.9±0.43 mm. In 14 patients with chronic pancreatitis these values were 24±10.5 HU, 44±25 HU and 2.0±0.54 mm, respectively. In a further group of 15 patients with chronic biliary disease, the values were 34±15 HU, 53±18 HU and 2.3±0.9 mm. The degree of wall enhancement was statistically significant in each group. There was no statistical difference in the attenuation characteristics or wall enhancement between normal patients and those with chronic pancreatitis. Patients with chronic biliary disease had a thicker gallbladder wall with higher attenuation before contrast but a similar degree of enhancement.

Contrast enhancement of the gallbladder wall has been reported on computed tomography (CT) in acute cholecystitis (Solomon et al, 1979; Kane et al, 1983), acute pancreatitis (Somer et al, 1984), gallbladder carcinoma (Thorsen et al, 1984) and following angiography where the gallbladder was considered to be normal (Strax et al, 1982). In the pathological conditions the degree of enhancement was considered abnormal. An acceptable range of normal enhancement does not appear to have been defined.

The thickness of the gallbladder wall has been measured on conventional tomography during contrast infusion, the reported normal thickness being less than 1 mm (Moncada et al, 1977a). This value has been used by some for assessment of the gallbladder by CT (Solomon et al, 1979), while others have used 2 mm (Somer et al, 1984) and 3 mm (Smathers et al, 1984) as the upper limit of normal. Engel et al (1980) found by ultrasound that a wall thickness of more than 3.5 mm was highly accurate in predicting the presence of gallbladder disease. This value has since been used in CT studies (Thorsen et al, 1984) but, because of technical and physical factors, measurements obtained by ultrasound may not be applicable to CT. In order to assess the thickness and degree of enhancement of the gallbladder wall in normal subjects, we have retrospectively studied all patients who underwent upper abdominal contrast-enhanced CT in this department in 1 year. The results in the normal patients were compared with data from patients with chronic biliary disease or with chronic pancreatitis.

PATIENTS AND METHODS

Clinical and CT data from 114 consecutive patients who had upper abdominal CT with and without intravenous contrast enhancement were reviewed. Seventy-seven patients were suitable for further study. Twenty had undergone cholecystectomy and 17 were excluded because of degraded CT images. The suitable patients were divided into three groups according to clinical and radiological information (Table I):

(1) no evidence of biliary or pancreatic disease (normal);
(2) chronic pancreatitis;
(3) chronic biliary disease.

Of the patients with chronic pancreatitis, the disease in two was clinically related to chronic cholecystitis and four were alcoholic but in the remaining eight patients no cause for their chronic pancreatitis had been determined.

Patients were not instructed to fast although, in practice, patients had not eaten for about 2 h before examination. Computed tomography was performed using an IGE 8800 general-purpose scanner. Patients received 100 ml of meglumine iothalamate (Conray 280, May & Baker Ltd) intravenously over 50 s by pump injection. Scanning commenced 20 s after the start of injection. Images were selected from the pre- and post-contrast CT examinations in order to demonstrate the maximum short-axis diameter of the gallbladder. The images were magnified and viewed at a

TABLE I

DETAILS OF PATIENTS

Group	No. of patients	Mean age (years)	Sex	
			Male	Female
Normal	48	49	26	22
Chronic pancreatitis	14	53	13	1
Biliary disease	15	58	9	6

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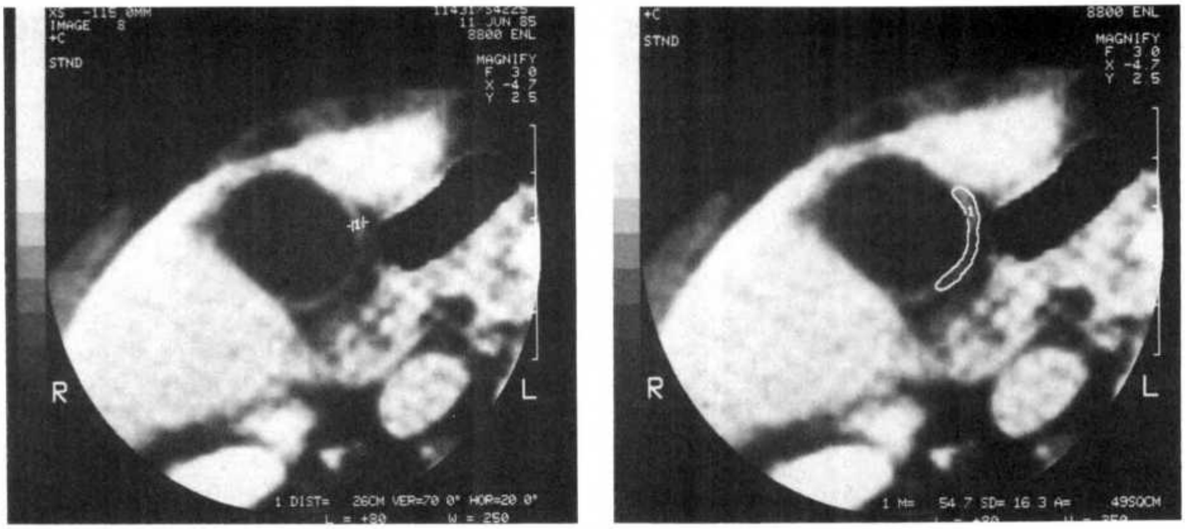
*Author for correspondence and reprints.



A B

FIG. 1.

A normal gallbladder wall on contrast-enhanced CT illustrating the measurement of (A) wall thickness and (B) attenuation (L + 80, W 250).

window width of 250 HU and a window level of 80 HU. The margins of a portion of the gallbladder wall which was clearly outlined by fat were carefully delineated. The thickness and attenuation of this region was measured by the computer as illustrated in Fig. 1. The attenuation of the gallbladder contents was measured before and after intravenous contrast enhancement to assess uniformity of measurement. The results were analysed using the Student's t-test for matched pairs to assess attenuation changes after contrast and the t-test for unpaired samples to compare the results in the three groups of patients.

RESULTS

The age distributions of the three groups of patients were not significantly different ($p > 0.05$; Table I). The sex distributions were similar, except that 13 of the 14 patients with chronic pancreatitis were male. Analysis of the data allowing for this difference did not affect the results or conclusions.

The three groups of patients all showed a significant degree of gallbladder wall enhancement after contrast ($p < 0.01$; Table II). In the clinically normal group the gallbladder wall thickness was less than 2.8 mm in over 95% of cases (mean + 2 standard deviations). There was no significant difference in thickness ($p > 0.05$) or attenuation, either before or after contrast ($p > 0.05$), between normal patients and those with chronic pancreatitis. Patients with biliary disease had thicker gallbladder walls compared with normal ($p < 0.05$) with a significantly higher pre-contrast attenuation ($p < 0.05$), but enhancement was of the same magnitude. The characteristics of the gallbladder contents did not change after injection of contrast medium.

DISCUSSION

The IGE 8800 CT scanner has a 320 × 320 pixel matrix, each pixel being 1.4 mm square. This measurement is greater than the normal gallbladder wall thickness found on conventional contrast-infusion tomography (Moncada et al, 1977a). The gallbladder wall may pass through several voxels in a 1 cm thick section due to its obliquity and curvature, therefore, the upper limit of normal for thickness of the gallbladder wall on CT will be greater than one pixel width (1.4 mm). While magnification of the image on the CT display permits precise cursor positioning, accuracy of measurement may not be improved because of computer-generated smoothing of the pixel margins.

TABLE II

GALLBLADDER WALL THICKNESS AND ATTENUATION BEFORE AND AFTER ENHANCEMENT WITH INTRAVENOUS CONTRAST MEDIUM

Group	Gallbladder wall thickness (mm)	Wall attenuation (HU)	
		Pre-contrast	Post-contrast
Normal	1.9 ± 0.43	25 ± 13	42 ± 18†
Chronic pancreatitis	2.0 ± 0.54	24 ± 10.5	44 ± 25†
Biliary disease	2.3 ± 0.9*	34 ± 15*	53 ± 18†

Figures expressed as mean ± standard deviation.
*Significantly different from normal ($p < 0.05$).
†Significantly different from the pre-contrast level ($p < 0.01$).

Determination of the wall margins is subjective and influenced not only by the window width and level of the image but also by the contrast between the wall and surrounding structures. We have attempted to minimise these factors by using the standardised technique described above and have found that, in 95% of normal patients, the gallbladder wall thickness is 2.8 mm or less. On scanners with a 512×512 pixel matrix, resolution is improved and the normal gallbladder wall thickness may be less. Because of the technical limitations placed on the assessment of wall thickness by pixel size and slice thickness, we feel that the normal range of wall thickness is unlikely to be significantly affected by the difference in the degree of distension of the gallbladder due to an incomplete period of fasting.

Measurement of attenuation from regions of interest on a magnified image uses computer-adjusted values from parts of adjacent pixels included in the region studied. However, by using careful delineation of a free edge of the gallbladder wall, alteration in attenuation after contrast is easily detectable. We have shown that after intravenous contrast, enhancement by approximately 20 HU is normal. Sophisticated and highly accurate methods are available for boundary detection on CT images (Zhu et al, 1986) but these methods are not widely available in clinical radiological practice. Pedrosa et al (1981) and Havrilla et al (1978) have both described gallbladder wall thickening in patients with chronic pancreatitis but do not indicate the clinical aetiology of the pancreatic disease. In our patients with chronic pancreatitis there was no significant difference in wall thickness or in attenuation compared with normal patients. This is probably because only two of our patients had gallbladder disease as a clinical cause of chronic pancreatitis. In idiopathic or in alcoholic pancreatitis the gallbladder appears normal on CT.

The group of patients with biliary disease did not include acute inflammatory disorders, where increased attenuation has been produced experimentally after injection of contrast medium (Moncada et al, 1977b). This may account for our observation of a thicker gallbladder wall without increase in the degree of contrast enhancement compared with that seen in the normal gallbladder. The increased wall attenuation before contrast medium is a reflection of the greater wall thickness, reducing the partial volume effect of surrounding lower-attenuation structures.

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REFERENCES

ENGEL, J. M., DEITCH, E. A. & SIKKEMA, W., 1980. Gallbladder wall thickness: sonographic accuracy and relation to disease. *American Journal of Roentgenology*, *134*, 907–909.

HAVRILLA, T. R., REICH, N. E., HAAGA, J. R., SEIDEMANN, F. E., COOPERMAN, A. M. & ALFIDI, R. J., 1978. Computed tomography of the gallbladder. *American Journal of Roentgenology*, *130*, 1059–1067.

KANE, R. A., COSTELLO, P. & DUSZLAK, E., 1983. Computed tomography in acute cholecystitis. New observations. *American Journal of Roentgenology*, *141*, 697–701.

MONCADA, R., CARDOSO, M., DANLEY, R., RODRIGUEZ, J., KIMURA, K., PICKLEMAN, J. & BRANDLY, J., 1977a. Acute cholecystitis: 137 patients studied by infusion tomography of the gallbladder. *American Journal of Roentgenology*, *129*, 583–585.

MONCADA, R., CARDOSO, M., DANLEY, R., RODRIGUEZ, J., KIMURA, K., PICKLEMAN, J. & BRANDLY, J., 1977b. Infusion tomography of the gallbladder: mechanism of gallbladder wall opacification in experimental acute cholecystitis. *American Journal of Roentgenology*, *129*, 587–590.

PEDROSA, C. S., CASANOVA, R., LEZANA, A. H. & FERNANDEZ, M. C., 1981. Computed tomography in obstructive jaundice. *Radiology*, *139*, 627–645.

SMATHERS, R. L., LEE, J. K. T. & HEIKEN, J. P., 1984. Differentiation of complicated cholecystitis from gallbladder carcinoma by computed tomography. *American Journal of Roentgenology*, *143*, 255–259.

SOLOMON, A., KREEL, L. & PINTO, D., 1979. Contrast computed tomography in the diagnosis of acute cholecystitis. *Journal of Computer Assisted Tomography*, *3*, 585–588.

SOMER, K., KIVISAARI, L., STANDERTSKJOLD-NORDENSTAM, C.-G. & KALIMA, T. V., 1984. Contrast enhanced computed tomography of the gallbladder in acute pancreatitis. *Gastrointestinal Radiology*, *9*, 31–34.

STRAX, R., TOOMBS, R. D., KAM, J., RAUSCHKOLB, E. N., PATEL, S. & SANDLER, C. M., 1982. Gallbladder enhancement following angiography: a normal CT finding. *Journal of Computer Assisted Tomography*, *6*, 766–768.

THORSEN, M. K., QUIROZ, F., LAWSON, T. L., SMITH, D. F., FOLEY, W. D. & STEWART, E. T., 1984. Primary biliary carcinoma: CT evaluation. *Radiology*, *152*, 479–483.

ZHU, X. P., CHECKLEY, D. R., HICKEY, D. S. & ISHERWOOD, I., 1986. Accuracy of area measurements made from MR images compared with computed tomography. *Journal of Computer Assisted Tomography*, *10*, 96–102.

Book reviews

Brigham and Women's Hospital Handbook of Diagnostic Imaging. Ed. by B. J. McNeil and H. L. Abrams, pp. 342, 1986 (Little, Brown and Co., Boston and Toronto), £15.40.
ISBN 0-316-56322-6

This pocket-sized compendium is a distillation of current radiological practice at a transatlantic centre of excellence. The approach is problem orientated, taking 62 clinical situations as the starting point. The diagnostic work-up of each problem is outlined by an algorithm to a point where investigation is complete. Brief comments enlarging on the role of each examination to the particular clinical situation, including its drawbacks, are followed by data on its sensitivity and specificity. The contribution of magnetic resonance imaging is included and, finally, there is a list of key references for each problem.

While this rigid, stepwise approach to diagnosis provides a helpful guideline for the mainstream of clinical cases, its limitations are likely to be exposed in practice by cases with conflicting findings or subtle nuances. For instance, rupture of a Baker's cyst is not included in the section on acute leg pain. Some interesting differences between American and British approaches become evident. An example is that more use seems to be made of lymphography and gallium scanning in cases of lymphoma and, probably, lymphography in testicular tumours than in the UK. Some recommendations are questionable, such as a barium enema in cases of suspected acute appendicitis or acute diverticulitis and the use of oral cholecystography in acute cholecystitis. The investigation of dyspepsia is a surprising omission, while needle biopsy in the investigation of a solitary pulmonary nodule requires amplification.

This book meets its stated aim as a reference source for non-radiologists. One suspects that outside the United States it will be radiologists, particularly those preparing for examinations, who will be most likely to appreciate its value as an up-to-date precis of imaging methods in day to day practice and a useful source of references.

G. H. WHITEHOUSE

Emergency Radiology of the Acutely Ill or Injured Child, 2nd edit. By L. E. Swischuk, pp. 622, 1986 (Williams and Wilkins, Baltimore), £72.
ISBN 0-683-08049-0

Dr Swischuk is obviously a very knowledgeable, hard-working, literal man, whose text provides exactly what the title and preface state: "bread and butter" radiology for the casualty officer or the doctor "on-take". The second edition has been enlarged from 496 to 622 pages by the addition of ultrasound and nuclear medicine. The discussions on trauma and infection in the chest, skeleton, abdomen, spine, and head and face are very good and, indeed, would be very applicable to much adult radiology. The emergency doctor who has mastered this text should have no imaging problems with his very acute patients.

Unfortunately, by Dr Swischuk's definition, a child seems to be about 1 year old, so there is no discussion of the acute congenital or infantile conditions that also present as emergencies. However, very good sections on intussusception and malrotation compensate for this.

The book is well produced and the illustrations are very good: miliary tuberculosis shows up perfectly and there is a good list of references.

There are the occasional differences in interpretation: the ultrasound illustrations in Figs 3.102 and 3.103 I would regard as diagnostic of splenic trauma and haematoma and as highlighting the benefits of the technique in the acutely injured patient. Dr Swischuk finds the ultrasound appearances either misleading or non-specific. As would be expected from an American text, there is more reliance on computed tomography than in the UK.

The second edition is up to date and as good as the first, and should prove just as useful to the emergency doctor in casualty, but it does need a supplementary text for the very young child.

G. M. STEINER

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Evaluation of an anatomical compensation filter for chest radiography

By *Hannu Manninen, M.D., M.Sc., Hannu Rytkönen, M.D., Seppo Soimakallio, M.D., †Erkki O. Terho, M.D. and Juha Hentunen, M.Sc.

Department of Diagnostic Radiology and †Pulmonary Diseases, University Central Hospital of Kuopio, SF-70210 Kuopio, Finland

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ABSTRACT

An anatomical compensation filter for improving the radiographic demonstration of the mediastinal and retrocardiac areas of a chest radiograph has been evaluated. The filter, made of a transparent, light-weight lead-plastic material was attached to the X-ray collimator housing. The device reliably improved the visibility of normally underpenetrated areas without producing detectable artefacts, provided the patient was correctly positioned. Hilar structures were also slightly better visualised. At the same time there was no statistically significant deterioration in visualisation of peripheral pulmonary vessels or parenchymal structures. Rib details and pleural calcifications were less well seen, however, a result that was to be expected because of the X-ray beam hardening.

It is difficult to achieve an acceptable distribution of density over the whole of a frontal chest radiograph because of great differences in X-ray absorption in various parts of the thorax. In particular, mediastinal, retrocardiac and subdiaphragmatic areas are often underexposed unless the lung fields are overexposed. The problem can be partly solved by the use of wide-latitude, single-emulsion films (Miller, 1980) or high-kV (250–350 kVp) techniques (Hallenbeck, 1975; Proto & Lane, 1978; Herman et al, 1982). The use of adjunctive "overpenetrated" views (Tuddenham, 1963) or photographic unsharp masking (Sorenson et al, 1981) requires an additional radiograph and they are time- and film-consuming procedures. A slit scanning equalisation system proposed by Plewes and Wandtke (1982) requires a complicated scanning beam, collimator-detector apparatus, and has the disadvantage of long scanning time. Digital computer techniques, though developing rapidly, still suffer from limited spatial resolution due to pixelisation (Giger & Doi, 1984) and require extensive instrumentation. Perhaps the simplest and cheapest approach to the problem is to place tailored filters in the X-ray beam at the tube portal which compensate for the patient's shape and achieve a balanced X-ray exposure across the chest image (Lynch, 1965; Wilkinson & Fraser, 1975; Garofiglio, 1983; Vyborny & MacMahon, 1984).

All these methods improve the visibility of retrocardiac and mediastinal structures (Tuddenham, 1963; Hallenbeck, 1975; Proto & Lane, 1978; Sorenson et al, 1981; Wieder & Adams, 1981; Wandtke & Plewes, 1983; Garofiglio, 1983) and result in higher nodule detection rates in these normally poorly penetrated areas when compared with conventional techniques (Armstrong et al, 1983; Ishida et al, 1984). The effect of these techniques on the visibility of anatomical structures in the lung fields has received less attention. In addition, these techniques have an effect on exposure times and/or X-ray beam quality (as regards the half-value layer, fraction of scattered radiation and contrast transfer), which might also be of clinical importance.

In the present study the effect of exposure equalisation on the visibility of various anatomical details was evaluated by investigating a commercial anatomical compensation filter for chest radiography (Du Pont), both in phantom experiments and in clinical radiography.

APPARATUS AND METHODS

Radiographic equipment

A three-phase, six-pulse generator (Philips DA 1000) with a Philips Rotalix SRO 03 100 tube and nominal focal spot of 1.2 mm was used. Total filtration was 2.5 mm Al. A 10 : 1 aluminium interspaced, stationary 40 lines/cm grid focused at 1.8 m and an automatic timer were used. Exposures were made at 125 kVp at a target–film distance of 200 cm. A medium-speed rare-earth screen (Trimax T4) with green-sensitive, high-contrast film (Trimax XD) was used for the study. The films were developed in an automated 90 s processor and the developing conditions were controlled with test films (Agfa Gevaert System Control RP 79001A). A commercial compensation filter for chest radiography (Du Pont) made of special, transparent, light-weight lead-plastic material tailored to match the shape of the lung fields was attached to the housing of the X-ray tube (Fig. 1). The height of the filter is 7 cm and the edges of the lung-field plates are gently sloping. If required, the device can be mounted at a distance from the tube housing and is easily removed from the X-ray beam. The filter corresponds to 0.1 mm Pb filtration in the lung fields. As radiographed in a 20 cm-thick water phantom, a density difference of 0.55 was found (at the monoexponential portion of the H-D curve of Trimax T4/XD screen-film combination) across the filter edge.

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*Author for correspondence and reprint requests.

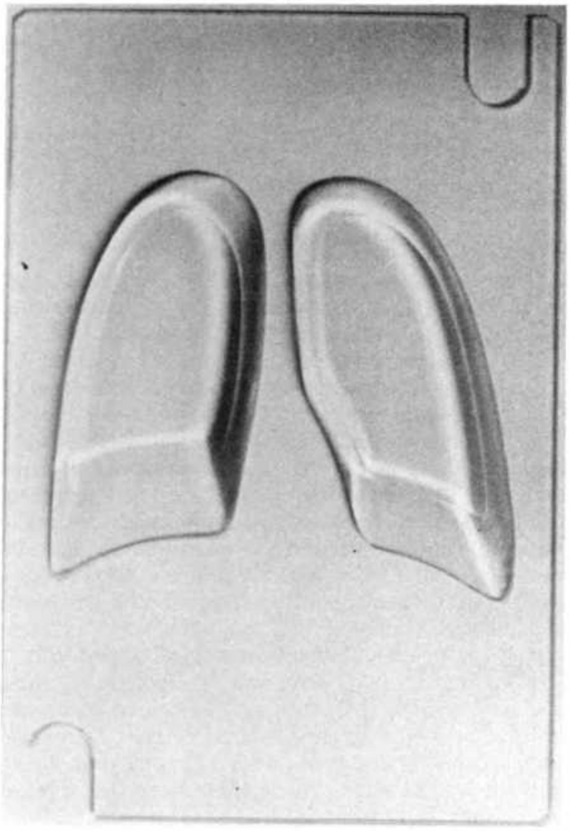


Fig. 1.

The anatomical compensation filter for chest radiography made of transparent, light-weight lead-plastic material (Du Pont).

Clinical chest radiographs

Postero-anterior chest radiographs were taken of 30 volunteers both with and without the filter. The volunteers were mainly patients with chronic heart disease or lung carcinoma (mean age 72 years, range 57–87 years). The filter was fixed at a set distance from the collimator housing and routine patient positioning procedure was applied. A metal test-plate was taped firmly on each person's back over the right upper lung and mediastinum. The plate consisted of randomised E letters corresponding to resolution of 0.2–5.8 line pairs/mm in three contrast zones. The test figures, made of gold, had been etched on a thin layer of copper and corresponded to 2.5 μm, 7 μm and 32 μm of Au (Laasonen, 1968). To eliminate the possible effect of film density differences on the results, film pairs with more than a 0.1 density difference as measured on a standard location over the left upper lung were rejected from the study. A Repromaster RM 21 densitometer with a 1 mm-diameter aperture was used for the density measurements. Since the degree of inspiration was required to be strictly identical for both radiographs of each pair, radiographs of 26 persons only were suitable for the final analysis. Entrance skin exposures were measured subsequently with a dosemeter (Ionex 2500/3) and an ionisation chamber by exposing an Alderson chest phantom.

Image analysis

Inherent subject contrast. The inherent (or visual) subject contrast (C_s) of the 32 μm-thick gold test-plate in the area of both the mediastinum and the lung field was calculated from the density values of each radiograph by the formula (Hale & Mishkin, 1969)

$$C_s = (10^{-D_o} - 10^{-D_a})/(10^{-D_o} + 10^{-D_a})$$

where D_o is the density of the object and D_a is the density of an adjacent area of the mediastinum or lung, respectively. The value for C_s was obtained as a mean of the measurements from all of the radiographs. Theoretically, the C_s of a low-contrast object represents an illumination contrast on the observer's retina, provided that one operates above the threshold limitations of the human eye as regards object size and illumination level (Lassen & Bloch, 1978).

E test-plate analysis. For the further E test-plate analysis, the films were randomised and assigned by code numbers. The radiographs were read by three observers with normal visual acuity on a conventional viewing box masked to the film size. The room illumination was dim and kept constant. The smallest E with a resolved opening direction was registered. An index of image quality was obtained as a mean of the film scores of the three contrast zones averaged over all observers, and it is referred to here as the visual detectability, D_v.

Visual assessment of the radiographs. For the visual analysis the radiographs of each patient were arranged in pairs. Radiographs were marked with a code number but could not be identified by the observers. For each pair the reference radiograph was selected at random, but in the data analysis the radiographic scores were calculated with reference to the conventional technique. For each film pair seven rectangular regions of interest (side length 4–8 cm) were masked with black films. In each region one anatomical or pathological feature (parameter) was assessed, except that rib visibility was evaluated in the same area as that of peripheral pulmonary vessels. The parameters are shown in Table I. Because of the age of the patients and the presence of lung or heart disease, the radiographs almost invariably showed some parenchymal pathology, usually reticular or rounded opacities. The visibility of these was assessed in the left lower zone and the result recorded as the parameter "parenchymal structures". The parameters were chosen to cover various regions of the chest: three evaluated the mediastinal and retrocardiac area, one the hilar region and three the lung fields. The parameter "clinical findings" included 12 calcifications of the aortic arch

TABLE I

THE ANATOMICAL/PATHOLOGICAL PARAMETERS EVALUATED FROM THE CHEST RADIOGRAPHS

Anatomical/pathological parameter	Abbreviation
Visibility of:	
Peripheral lung vessels of left upper lung	Vascularity
Parenchymal structures of left lower lung	Parenchyma
Retrocardiac pulmonary vessels	Retrocardiac area
Vertebral body in the middle third of the thoracic spine	Vertebra
Tracheal bifurcation	Bifurcation
Pulmonary hilum	Hilum
Rib details of left upper thoracic wall	Ribs
Clinical findings	Findings

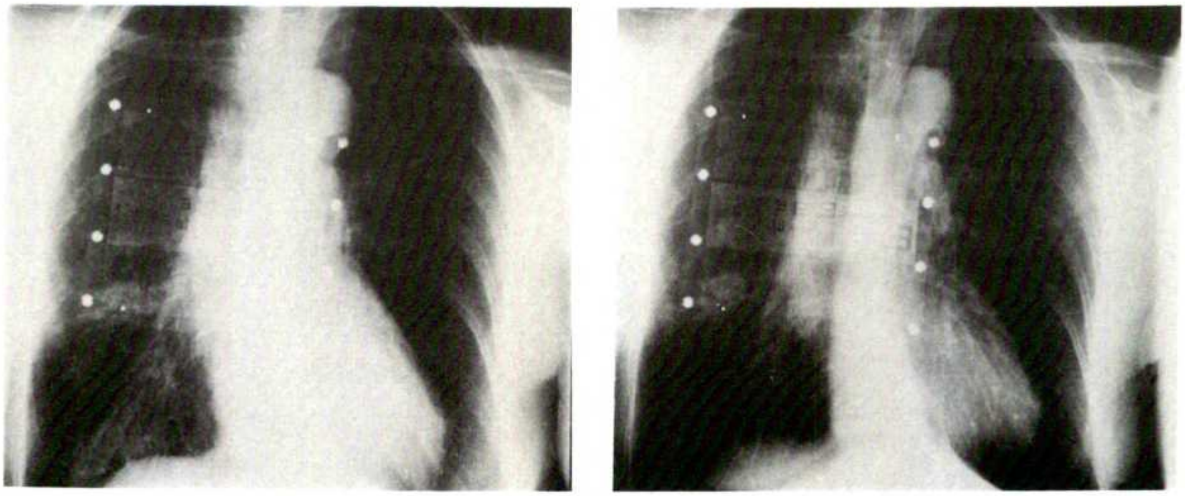
and nine cases of pleural calcifications and shadowing, the rest being mass lesions and findings associated with cardiac insufficiency.

In the visual assessment four observers—one senior radiologist (S.S.), one senior chest physician (E.O.T.), and two residents in radiology (H.R. and H.M.)—graded the quality of each film compared with the reference radiograph. Thus the film score of each anatomical parameter was a mean of 104 comparisons, the total number of observations being 832. The scoring system used was: $+2$ = clearly better, $+1$ = slightly better, 0 = equal, -1 = slightly worse, and -2 = clearly worse than the reference radiograph. Viewing time and distance were not restricted. The reproducibility of this kind of visual grading analysis has been found to be sufficient for comparison of imaging techniques in clinical chest radiography (Manninen et al, 1984; Manninen, 1985a). For statistical comparisons of the film scores a paired t-test was applied.

To test the adequacy of the density requirement for the film pairs (density difference not more than 0.1, giving mean density difference 0.02 as measured on the left upper lung field), a non-parametric Kendall correlation coefficient was calculated between each film score and density difference of the corresponding films, averaged for all observers. Statistically significant correlations were not found for any anatomical/pathological parameter.

Results

Figure 2 shows a typical pair of chest radiographs obtained with the conventional grid technique and with the chest filter arrangement. The mediastinal and retrocardiac areas are underexposed with the conventional technique while clearly better visualisation was obtained by the use of the filter. Table II gives the mean exposure times and patient exposures as well as the values of inherent subject contrast for the E test-plate in the mediastinum and the lung field. The exposure times as well as the skin exposures over the mediastinum for the filter technique were 1.8 times those for the conventional chest radiography, while on the lung fields the skin exposure with the former arrangement was only 0.7 times that for the latter technique. The object contrast with the filter technique was about twice as good in the mediastinal area but slightly worse in the lung field compared with the conventional technique. Table II also gives the values of the visual detectability of the E test-plate. The superiority of the conventional technique over the filter arrangement as measured with the E test-plate D_v values was highly significant ($p < 0.001$) for all contrast zones, and the D_v values of



A

B

Fig. 2.

A pair of chest radiographs obtained (A) by the conventional and (B) by the filter arrangement.

TABLE II

THE MEAN EXPOSURE TIMES, SKIN RADIATION DOSES, AND VALUES OF C_s AND D_v OF THE GOLD E-TEST-PLATE IN THE CLINICAL CHEST RADIOGRAPHS

Technique	Mean exposure time (ms)	Skin dose (μGy) over		C_s		D_v (line pairs/mm)
		mediastinum	lung	mediastinum	lung	
T4/XD	25	260	250	0.04	0.29	1.52
T4/XD filter	45	470	180	0.08	0.24	1.33

C_s = inherent subject contrast, D_v = visual detectability.

individual observers did not differ significantly from each other.

Table III shows the average score for all observers of each parameter with the filter technique (the scores for the conventional technique being graded as 0), as well as the significance of the differences between the techniques. Figure 3 presents the film scores given by individual observers for each parameter. Table III and Fig. 3 indicate clearly the superiority of the filter technique as regards visibility of the mediastinal (both bony structures and air–tissue borders) and retrocardiac areas. Also, hilar structures were slightly better visualised with the filter arrangement. There was no significant difference in visibility of structures in unobscured lung fields as assessed by peripheral vessels and parenchymal (interstitial type) shadowing or in the visualisation of aortic arch calcification. On the other hand, rib details and pleural calcifications were not as

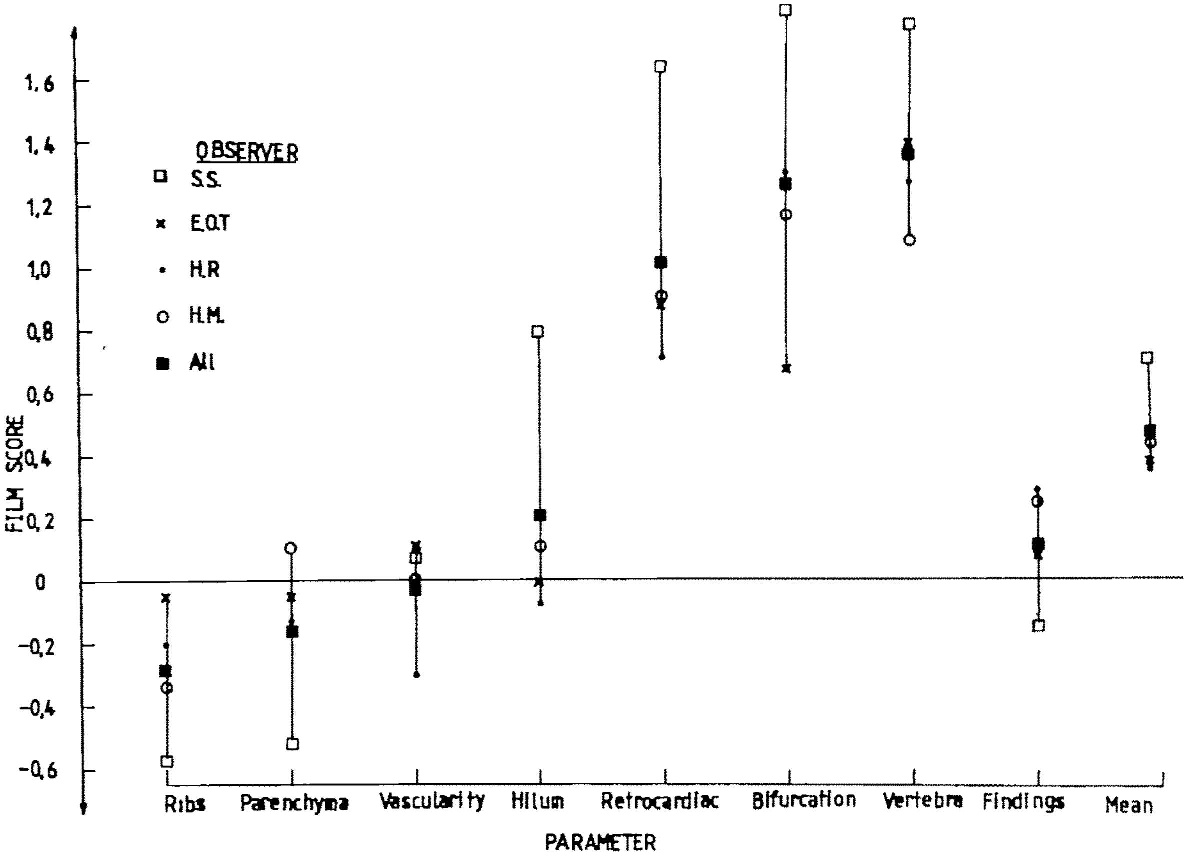


FIG. 3.

The film scores of the filter technique given by individual observers for each anatomical/pathological parameter.

TABLE III

The radiographic scores averaged for all observers for each parameter using the filter arrangement (conventional radiography graded as 0) and significance of the scores with filter compared with the conventional technique

Anatomical/pathological parameter*	Film score
Vascularity	−0.02 NS
Parenchyma	−0.15 NS
Retrocardiac area	1.03†
Vertebra	1.38†
Bifurcation	1.25†
Hilum	0.21§
Ribs	−0.30†
Findings	0.10 NS
Aortic calcifications	0.04 NS
Pleural calcifications	−0.61†
Combined mean film score	0.43†

*Abbreviations of parameters from Table I. †$p < 0.001$; ‡$p < 0.01$; §$p < 0.05$; NS $p > 0.05$.

well visualised with the filter arrangement. Figure 3 shows that there was considerable interobserver variation in the scores given to the individual parameters. This resulted in statistically significant differences between individual observers as regards scores for visualisation of tracheal bifurcation, vertebral body, and hilar regions. There were, however, no statistically significant disagreements between individual observers with regard to the order of superiority of the techniques for any parameter.

The borders of the filter were not detectable on any of the chest radiographs. Good visualisation of the mediastinal and retrocardiac structures was obtained in all but two patients. Both patients had had heart failure, had very large hearts and had taken shallow inspirations. Deformities of the thoracic cage, especially severe scoliosis, invalidate the use of the filter

Discussion

There are two mechanisms by which an anatomical compensation filter has an equalising effect on the density distribution of a chest radiograph. Firstly, the filter absorbs X rays over the lung fields and makes the exposure distribution across the whole chest radiograph more uniform. Secondly, the filter makes the X-ray beam more penetrating and reduces contrast in the lung fields (see Table II), thus further improving image latitude. Theoretically, decrease in visual subject contrast is partly due to a reduced X-ray attenuation coefficient and partly due to an increased fraction of scattered radiation reaching the image plane (Johns & Cunningham, 1983). Contrast of bony structures is especially decreased, because the X-ray attenuation coefficient of bone, relative to that of soft tissue, decreases more rapidly (Spiers, 1946). The latter phenomenon is analogous to that in high-kV techniques, but observations about its effect on visibility of clinically important details are still conflicting (Hallenbeck, 1975; Proto & Lane, 1978; Herman et al, 1982). Another consequence of the X-ray beam hardening is the increased proportion of emitted K-edge photons from the screen phosphor, reabsorption of which decreases spatial resolution (Arnold & Bjärngard, 1979), a fact that might decrease visibility of minute details on the lung fields. Finally, by decreasing X-ray beam intensity, the filter arrangement requires longer exposure times, and thus kinetic blurring, especially in the hilar regions, might become disturbing. In the present study, only one compensation filter was evaluated, but because of the identical basic operating principles, the results are probably applicable to variable-thickness chest filters as a whole.

As expected, visibility of mediastinal and retrocardiac structures was clearly better with the filter arrangement compared with conventional radiography. This is due to increased depth resolution (*i.e.* reduced thickness of tissue that will cast a detectable shadow) when the density of these areas gets out of the "toe" region of the H-D curve of the screen-film combination (Dyke et al, 1975) By using the filter the inherent (or visual) subject contrast of a 32 μm-thick gold plate increased by a factor of two (Table II).

Because of the X-ray beam hardening, the visual subject contrast of the gold plate decreased slightly in the lung fields (Table II). Decrease in the visual detectability of the E test-plate figures was also noticed with the filter. The D_v of the gold E test-plate radiographed on the human chest has previously been found to correlate closely with the resolution capacity of the imaging chain (Manninen, 1985b). Clinically, reduced visibility of rib details and pleural calcifications was noticed (Table II). However, visualisation of the calcifications of the centrally situated aortic arch was not impaired. Practically identical visualisation of peripheral pulmonary vessels was registered, while detectability of parenchymal changes was slightly, though not statistically significantly, poorer with the filter arrangement. The result contradicts the finding of Proto and Lane (1978) that X-ray beam hardening, using high-kV techniques, improved detection of interstitial disease. Wieder and Adams (1981), using an aluminium trough filter, did not find any change in the visibility of "parenchymal" shadows.

In the hilar region, the visibility of anatomical details was slightly improved by the use of the filter (Table III). This implies that the improvement from the equalising effect of the filter on exposure distribution also in this region exceeds decrease in image quality due to increased motion unsharpness caused by longer exposure times. In fact the exposure times (see Table II) did not exceed recommended maximal values for chest radiography (Meredith & Massey, 1972). For ideal visualisation of hilar and paravertebral structures accurate patient positioning is important to avoid artefacts caused by the filter edge, and for patients suffering from severe scoliosis or other severe deformities of the thoracic cage the technique should not be applied.

The filter arrangement generally obtained a clearly better score for the combined mean value of the eight quality parameters (three of which described visibility of mediastinal and retrocardiac structures, one visibility of hilar regions, three visualisation of peripheral lung fields, and the parameter "clinical findings" for the whole area of the chest radiograph). Though the usefulness of an anatomical compensation filter in diagnosing chest pathology is a very complicated question and depends on the clinical problem being investigated, it is evident that the technique provides a reliable and simple way to improve the visibility of normally underpenetrated areas of the chest radiograph without significant impairment of the visualisation of the lung fields.

REFERENCES

Armstrong, J. D., Sorenson, J. A., Nelson, J. A., Tocino, I., Lester, P. D., Janes, J. O., Niklason, L. T. & Stanish, W., 1983. Clinical evaluation of unsharp masking and slit scanning techniques in chest radiography. *Radiology, 147*, 351–356.

Arnold, B. A. & Bjärngard, B. E., 1979. The effect of phosphor K x-rays on the MTF of rare-earth screens. *Medical Physics, 6*, 500–503.

Dyke, W. P., Barbour, J. P. & Charbonnier, F. M., 1975. Depth resolution: a mechanism by which high kilovoltage improves visibility in chest films. *Radiology, 117*, 159–164.

Garofiglio, G., 1983. Study of the mediastinum in routine thorax, using the air gap/filter compensation technique. *Proceedings of Vth European Congress of Radiology, Bordeaux, October 1983*, p. 83.

Giger, M. L. & Doi, K., 1984. Investigation of basic imaging properties in digital radiography. *Medical Physics, 11*, 287–295.

Hale, J. & Mishkin, M. M., 1969. Serial direct magnification cerebral angiography. Theoretical aspects. *American Journal of Roentgenology, 107*, 616–621.

Hallenbeck, G. S., 1975. Clinical evaluation of the 350 kV chest radiography system. *Radiology, 117*, 1–4.

Herman, P. G., Drummey, J., Swensson, R. G., Hessel, S. J. & Balikian, J. P., 1982. 350 kV chest radiography has no diagnostic advantage: a comparison with 140 kV technique. *American Journal of Roentgenology, 138*, 485–489.

Ishida, M., Doi, K., Loo, L.-N., Metz, C. E. & Lehr, J. L., 1984. Digital image processing: effect on detectability of simulated low-contrast radiographic patterns. *Radiology, 150*, 569–575.

Johns, H. E. & Cunningham, J. R., 1983. *The Physics of Radiology*, 4th edit. (Charles C. Thomas, New York, Springfield, Illinois).

Laasonen, E. M., 1968. Information transmission in roentgen-diagnostic chains: experiments and clinical studies. *Acta Radiologica*, Suppl 280.

Lassen, M. & Bloch, P., 1978. Theoretical considerations of effects of x-ray film-screen characteristics on threshold detectability of small low-contrast objects. *Medical Physics, 5*, 146–153.

Lynch, P. A., 1965. A different approach to chest roentgenography. Triad technique (high kilovoltage, grid, wedge filter). *Radiology, 93*, 965–973.

Manninen, H., 1985a. *Physical Image Parameters and Diagnostic Quality of Roentgenographs: Investigations on Chest Imaging Chains.* Academic Dissertation, Publications of the University of Kuopio, Medicine, Series Original Reports 1/1985.

——1985b. A three-contrast, metal test pattern (Snellen E-plate) in evaluation of imaging techniques in clinical chest radiography. *Acta Radiologica Diagnosis, 26*, 307–313.

Manninen, H., Terho, E. O., Wiljasalo, M., Wiljasalo, S. & Soimakallio, S., 1984. An evaluation of different imaging chains in clinical chest radiography. *British Journal of Radiology, 57*, 991–995.

Meredith, W. J. & Massey, J. B., 1972. *Fundamental Physics of Radiology*. 2nd edit. (John Wright & Sons Ltd, Bristol), p. 215.

Miller, T. D., 1980. Alternate approach to extending latitude, increasing definition and enhancing contrast in chest radiography. In *Optimization of Chest Radiography*. US Department of Health and Human Services HHS Publication (FDA) 80-8124, June 1980, pp. 72–80.

Plewes, B. D. & Wandtke, J. C., 1982. A scanning equalization system for improved chest radiography. *Radiology, 142*, 765–768.

Proto, A. V. & Lane, E. J., 1978. 350 kVp chest radiography: reviews and comparison with 120 kVp. *American Journal of Roentgenology, 130*, 859–866.

Sorenson, J. A., Niklason, L. T. & Nelson, J. A., 1981. Photographic unsharp masking in chest radiography. *Investigative Radiology, 16*, 281–288.

Spiers, F. W., 1946. Effective atomic number and energy absorption in tissues. *British Journal of Radiology, 19*, 52–63.

Tuddenham, W. J., 1963. Problems of perception in chest roentgenology: facts and fallacies. *Radiologic Clinics of North America, 1*, 277–289.

Vyborny, C. & MacMahon, M., 1984. Foil filters for equalized chest radiography. *Radiology, 151*, 524.

Wandtke, J. C. & Plewes, D. B., 1983. Improved chest radiography with equalization. *Radiographics, 3*, 141.

Wieder, S. & Adams, P. L., 1981. Improved routine chest radiography with a trough filter. *American Journal of Roentgenology, 137*, 695–698.

Wilkinson, G. A. & Fraser, R. G., 1975. Roentgenography of the chest. *Applied Radiology, 4*, 41–49.

1986, *The British Journal of Radiology*, 59, 1093–1098 NOVEMBER 1986

A feasibility study of a new approach to clinical radiosensitisation: hypothermia and hyperbaric oxygen in combination with pharmacological vasodilatation

By R. Sealy, F.R.C.R., *G. G. Harrison, M.D., *D. Morrell, F.F.A. (S.A.), †J. Korrubel, H.T.S., *A. Gregory, H.T.S., L. Barry, M.S.R., G. Blekkenhorst, Ph.D., †E. R. Hering, Ph.D., ‡A. B. Fataar, M.Med. (Nuc. Med.) and ‡J. Boniaszczuk, Dip. Rad.

Departments of Radiotherapy, *Anaesthetics, †Medical Physics and ‡Nuclear Medicine, Groote Schuur Hospital and University of Cape Town Medical School, 7925 Observatory, Cape Town, South Africa

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ABSTRACT

It is proposed that hyperbaric oxygen fails in the clinical situation due to a high proportion (greater than 33%) of hypoxic cells in human tumours The means of overcoming this problem are reviewed. Additional to hyperbaric oxygenation, moderate hypothermia (30°C) to allow redistribution of oxygen in the tumour is proposed. A system of externally controlled intravenous anaesthesia has been developed for the single-subject hyperbaric cylinder. Pharmacological vasodilatation is induced in the anaesthetised patient who is then fluid loaded and cooled. Initial single-sensitising treatments are advocated Twenty-nine patients with advanced mouth cancer have completed a course of this treatment, of whom five of nine were free of disease after 2 years and 10 of 21 at 1 year, with three intercurrent deaths. Fifteen have experienced local failure This approach would appear to be practical, safe and promising.

Hyperbaric oxygen in clinical radiotherapy has not fulfilled its early promise (Churchill-Davidson et al, 1957). It would appear that large tumour size adversely influences response (Van den Brenk, 1968; Chang et al, 1973; Henk et al, 1977; Henk & Smith, 1977; Sealy, 1979), even when subject to prior shrinkage with chemotherapy (Sealy et al, 1982). Similar results are seen in animal tumours (Suit & Maeda, 1967).

We postulate, therefore, that the poor response to irradiation in hyperbaric oxygen is a function of incomplete radiosensitisation due to an increased percentage of hypoxic cells present in tumours of a more advanced stage. Even small human tumour nodules may have 20–40% hypoxic cells (Denekamp et al, 1977). Murine tumours may have size-dependent hypoxic fractions (for a review, see Moulder & Rockwell, 1984), while Mueller-Klieser et al (1984) have shown that oxyhaemoglobin saturation by hyperbaric oxygen in tumour capillaries also depends upon tumour size. Our hypothesis is supported by the view of Adams (1978) in that a highly significant gain factor for a hypoxic radiation sensitiser treatment will only be seen when less than 0.001% of the tumour cells remain biologically hypoxic when so exposed. Hyperbaric oxygen at 3 atmospheres absolute increased the oxygen-carrying capacity of the blood by about 33% over that in air; thus, it would not be possible, under the most favourable conditions, to oxygenate completely tumours with a very high proportion of hypoxic cells by this means alone. Morgan (1967) has calculated, for a large tumour, that even 1% of hypoxic cells would increase the necessary radiation dose for cure to impossibly high levels for clinical tolerance. It is, therefore, appropriate to explore methods of achieving a several-fold improvement in the oxygen supply of tumours over that which is obtained in conventional hyperbaric oxygen at 3 atmospheres absolute. Increasing oxygen pressure of from 3 to 4 atmospheres raises the oxygen-carrying capacity of the blood by a further 12%. This would not be adequate if more than 45% of the cells were to be hypoxic in even a small area of a tumour.

Peripheral vasoconstriction (Whalen et al, 1965; Bachofen et al, 1971; Johnson, 1971; Johnson et al, 1972) may be an important unwanted side-effect of oxygen therapy which should be avoided in the clinical situation (Sealy, 1979) since it may be protective (Milne et al, 1973; Pallavicini & Hill, 1983). However, its abolition would not improve the supply of oxygen to the tumour more than about 33% above that seen in air (Whalen et al, 1965) and, thus, as a sole additional measure would not be expected to increase the radiation sensitivity of a cell population with greater than 33% hypoxic cells.

Another option is the use of hyperbaric oxygen together with a concomitant reduction in the oxygen utilisation rate of the tumour. This could lead to a centrifugal redistribution of oxygen within the tumour cord (Thomlinson & Gray, 1955) or layers (Scott, 1957). This condition can be achieved pharmacologically (Crabtree & Cramer, 1934; Hall et al, 1952; Durand & Biaglow, 1974; Haynes & Inch, 1976), but systemic doses of drugs in excess of those which can be given under ordinary clinical conditions would probably be required (Durand et al, 1976).

Address for correspondence: R. Sealy, Department of Radiotherapy, Groote Schuur Hospital, 7925 Observatory, Cape Town, South Africa.

Induced hypothermia provides an alternative approach. Crabtree and Cramer (1934) and Hall et al (1952) suggested that the radiation sensitivity of mouse tumours might be increased at 0°C. In an attempt to improve radiation sensitivity by causing a reduction in oxygen utilisation and, hence, a redistribution of available oxygen, Bloch et al (1961) irradiated moderately hypothermic patients for glioblastoma multiforme. but found radiation-induced brain oedema. In less critical anatomical situations this might not be a limiting factor. Surface physico-pharmacological cooling to about 30°C is well known in anaesthetic practice and cardio-pulmonary bypass cooling to about 14°C is frequently undertaken in cardiac surgery. As an initial study, we decided to investigate the former.

Two widely differing rates of change of oxygen utilisation with change in temperature are quoted in the literature (Bigelow et al, 1950; Ross, 1954; Horvath & Spurr, 1956; Wright, 1971; Ganong, 1983). Utilising the lower rate quoted (7%/1°C), it can be calculated that the whole-body oxygen consumption at 30°C will be of the order of 50% of what it is at 37°C This figure seems to have fairly wide acceptance (Bigelow, 1958; Nunn, 1980).

Cardiac output falls with drop in temperature and figures of 50% of normal at 28°C are quoted (Ross, 1954), but even were this to be so and peripheral perfusion decreased proportionately, 3 atmospheres absolute oxygen at 30°C would still effectively provide an excess of additional available oxygen.

If a tumour was fully oxygenated, and the dose for 37% cell survival was about 1.40 Gy, then a single dose of 6.00 Gy would leave a surviving fraction of less than 2%. It would be expected that the redistribution of oxygen following such massive cell death would allow effective reoxygenation of the surviving tumour cells, provided that the significant factor was not destruction of critical elements of the tumour vasculature.

We describe here our experience in 31 patients in whom radiosensitisation was achieved by hypothermia and hyperbaric oxygen (3 atmospheres absolute) in combination with pharmacological vasodilatation.

THE LOGISTICS OF PROVIDING ANAESTHESIA

The provision of an environment for radiotherapy of hyperbaric oxygenation and hypothermia poses pathophysiological and logistic problems, of which the former are the most serious. Of all the pathophysiological accompaniments of induced hypothermia, the most dangerous is cardiac arrhythmia, especially ventricular fibrillation, the threshold for which is usually below 30°C, the target temperature accordingly chosen.

Before treatment, all patients have myringotomy needles inserted. For the induction of hypothermia a standard technique of surface cooling under general anaesthesia is used. Because of the constraints of the hyperbaric cylinder, we have opted for total intravenous anaesthesia with a continuous infusion of etomidate (1–2 mg/kg/h) combined with fentanyl (300–400 μg during the period of cooling), paralysis with d-tubocurarine (approximately 45 mg during total period of anaesthesia) and ventilation with nitrous oxide with 40% oxygen during cooling and oxygen alone during the hyperbaric phase.

After induction of anaesthesia and immediately before commencement of cooling, vasodilatation and control of shivering is achieved by the administration of 20–50 mg of Largactil (May & Baker Ltd) administered with appropriate fluid loading (balanced salt solution and plasma). The patient's physiological homeostasis is controlled by appropriate reactions to monitoring of multiple vital functions. These include electrocardiography and arterial and venous pressure transduced from percutaneous radial arterial and right atrial cannulation. These allow also for serial monitoring of acid–base, blood–gas and electrolyte status. A separate intravenous line is established for fluid and drug infusion. End-tidal CO_2 concentration is continuously monitored by capnography, the volume of ventilation being adjusted to maintain end-tidal CO_2 concentration between 4% and 5% during the fall in temperature and metabolic rate. If necessary, 2–4% CO_2 is added to the inspired gas mixture during cooling to prevent alkalosis.

Temperature is monitored in the middle third of the oesophagus and in the rectum with thermistor probes.

A cooling rate of 1°C/15 min has been found to be optimal in terms of accurate control of afterdrop. Once the temperature has reached its nadir following afterdrop—which approximates 2°C—and oesophageal and rectal temperature have equilibrated, core temperature remains stable for a prolonged period.

Hyperbaric phase

Major logistical problems follow from the spatial constraints of our single-patient pressure vessel (Vickers Mark IV), the spark and explosion danger inherent in the hyperbaric oxygen environment and the enforced remoteness of the anaesthetist from the patient for the period of pressurisation and irradiation. Modifications of the cylinder door were made to permit airtight passage of intravenous lines for the administration of intravenous anaesthetics and other drugs from without by means of constant infusion pumps (IVAC), and cables from all the monitoring devices to appropriate external displays to allow continuous monitoring.

The period for which the patient is remote from the anaesthetist is of the order of 50 min.

Ventilation

Ventilation with pure oxygen in the tank is provided by a compact Vickers fluid logic ventilator. It has no moving parts and so obviates any danger of spark generation. Airway pressure generated during the inspiratory phase is registered on a pressure gauge inside the tank visible through the perspex wall and, together with the capnograph oscillation, provides a visible means of monitoring respiration.

Depressurisation, rewarming and reversal of neuromuscular block

At the conclusion of therapy, the patient is depressurised, removed from the tank and rewarmed in a bath of warm water.

Once rectal and oesophageal temperatures exceed 34°C, the action of muscle relaxant is reversed with glycopyrrolate/neostigmine, spontaneous respiration is re-established, anaesthesia discontinued and the patient allowed to awaken.

Complications

We have applied this technique on 42 occasions to 34 patients, the number of treatments per patient being dictated by radiotherapeutic criteria. All patients have regained consciousness rapidly after treatment and have been fit for discharge from hospital the next morning.

The most dangerous complication associated with induced hypothermia is the onset of various cold-induced cardiac arrhythmias, the incidence increasing sharply at temperatures below 30°C. Fifteen of the 42 treatments have been so complicated. These were, in order of frequency: atrial fibrillation (12), ventricular tachycardia (one), multiple ventricular premature systoles (one), ventricular fibrillation (one). Initially, aggressive attempts at increasing cooling rates resulted in poor control of afterdrop with a high incidence of arrhythmia, but with better control of cooling rates; only four instances of atrial fibrillation have occurred in the last 21 patients treated. Atrial fibrillation has reverted to sinus rhythm in all cases on rewarming, combined with Verapamil (Knoll, Ltd) 5 mg in all but three. The episodes of ventricular tachycardia and multiple ventricular premature systoles were controlled with lignocaine.

Cold-induced hypertension

A consistent reaction has been a hypertensive response of varying degree to the movement and handling of the cooled, vasodilated and fluid-loaded patient and his insertion into, and pressurisation in, the pressure vessel. We have found the continuous infusion of sodium nitroprusside of use in controlling this reaction. The subsequent warming hypotension secondary to vasodilatation is then relatively easily handled by discontinuing the drug and volume loading of the patient.

Cardiac output

The relative cardiac output was determined in six patients, using a radionuclide technique as previously described (Novitsky et al, 1984). Technetium-99m labelling of red blood cells was carried out *in vitro* using the Brookhaven National Laboratory Kit according to the method of Smith and Richards (1976). Activities of about 1500 MBq were used because of the necessity of accumulating a sufficient number of counts in as short a time as possible. A high-resolution, low-energy collimator on a Siemens gamma camera linked to a Medical Data Systems computer was employed, scanning in the anterior and left anterior oblique views.

The mean cardiac output in the conscious patient was 4.1 l/min (range 2.6–5.3 l/min) and in the anaesthetised, cooled, vasodilated, fluid-loaded patient was 4.7 l/min (range 3.5–6.2 l/min). These findings indicate that, under these conditions, decrease in the cardiac output did not occur.

Acid–base and fluid balance

No difficulties have resulted in relation to blood–gas and acid–base homeostasis, but the cold-induced diuresis, usually commencing at a core temperature of 31–32°C and which commonly leads to the passage of 2–3 l of dilute urine during the procedure, does require catheterisation and careful management, especially with regard to its effect on serum K^+ level and control of circulatory volume homeostasis.

Clinical Radiotherapeutic Experience

Patient selection

Since August 1982 the treatment has been offered to patients with Cape Town T_3 (4–6 cm), T_4 (in excess of 6 cm diameter) or N_3 (fixed nodes) histologically confirmed inoperable squamous carcinoma of the mouth. Such tumours thus tend to be larger than those staged as T_3 or T_4 in the International Union against Cancer (UICC, 1978) classification, since invasion of muscle or bone does not advance the Cape Town stage, which is calculated purely on size. It is our experience that about 25% of such patients are free of disease 1 year after conventional radiation treatment. Whilst being prepared for treatment, most patients received methotrexate intravenously (80 mg/m^2 body surface per week) to prevent extension of the tumour. It is our experience that such chemotherapy administered until about 1 week before irradiation does not affect subsequent radiotherapeutic control of the disease (Sealy et al, 1982).

The protocol was passed by our local ethical review committee and informed patient consent obtained.

Irradiation technique

An individual perspex cast was made for each patient and the known tumour and spinal cord localised within it. Individually drawn conventional multifield treatment plans were prepared and special attention given to avoidance of the spinal cord. The cast was made to fasten in a known position on the table top within the hyperbaric cylinder. To allow for refraction of the light beam, the set-up was rehearsed with the cast only, with a simulator of the hyperbaric cylinder on the treatment couch. This enabled the beam entry points and angles and the source–skin distances to be marked on the cast. Ellis-type compensators and a 1 cm build-up where the peak dose was required to be on the skin surface were made. Eight MeV X rays and the Vickers Mark IV hyperbaric cylinder at 3 atmospheres absolute on a modified hand-operated commercial hydraulic ram were used. The time taken to place the patient into the chamber averaged about 30 min; thus, patient placement took place when the core temperature was about 32°C. Afterdrop cooling continued during this placement period, as well as the compression and the soaking times (15 min). The intratumour treatment levels, as measured by interstitial thermistor probes, closely followed those of the core and were about 30°C in all cases, before and after irradiation. All patients, except the first, also received prophylactic neck nodal irradiation given in air at ambient temperature. The usual nodal dose was about 42 Gy in 14 fractions given three times per week.

Radiation fractionation

Large-fraction hypothermic hyperbaric radiotherapy to the known disease only was given at the beginning of the treatment course. Anaesthetic considerations prevented more than one such treatment per week and the original aim was, therefore, to deliver two fractions of 6.00 Gy tumour dose to produce a large cell kill on Treatment Days 1 and 7, with two fractions of 2.00 Gy on Days 3 and 4. However, it became clear that two hypothermic treatments were difficult to schedule and later only one initial treatment was given. Thereafter, five times weekly treatments in air at ambient temperature were given to clinical tolerance, usually 20 × 2.00 Gy with two hypothermic fractions (total dose 56.00 Gy in 37 days) and 26 × 2.00 Gy with one (total dose 58.00 Gy in 38 days). With a single hypothermic treatment, two booster daily doses of 3.00 Gy were usually given to any residual mass at the end of treatment. The respective TDF values were estimated to be about 95 and 100, and corrected for the hypothermic RBE to about 114 and 119, using the data obtained in the accompanying paper (Hering et al, 1986). Two patients, because of machine breakdown or the necessity to control hypertension, received hypothermic irradiation at the end of their course of radiation.

Radiation reactions

Our experience of acute post-irradiation oedema was similar to that of Bloch et al (1961). This appeared some 2–4 h after treatment and in the first patient was of such a degree that tracheotomy was performed as a prophylactic measure before the second treatment. All other patients were then controlled by a single dose of 100 mg of dexamethasone given intravenously at the time the anaesthetic was discontinued. The acute radiation reactions developing during the course of treatment were scored for erythema and membrane formation (Sealy et al, 1982) and did not differ from those experienced during conventional courses of treatment

With the exception of one patient with mandibular necrosis, marked late effects have not so far been seen. The large tumours treated have necessitated large fields which have resulted in mild to moderate xerostomia. Mild subcutaneous oedema has been seen in four patients but this has regressed in two. One patient has subcutaneous fibrosis at 28 months and another at 24 months.

In five patients who received two initial hypothermic treatments, the mean time to clinical tumour regression was 14.6 (range 7–21) days, whereas in 19 patients who received one such treatment the mean time was 39.3 (range 11–60) days.

Results of treatment

Thirty-one patients have accepted and completed a course of treatment. In two early cases hypothermic treatment was abandoned. Twenty-seven of 29 patients treated hypothermically experienced complete initial regression of the tumour. Five of nine hypothermically treated patients were free of disease after 2 years, whilst 10 of 21 patients at risk at 1 year remain free of disease. In addition, a further three patients have died free of disease in the treated area, of a cerebrovascular accident, lung metastases or pneumonia, possibly associated with lung metastases, less than 12 months after completing treatment. Eight patients completed hypothermic irradiation less than 1 year ago. Compared with a series of 64 consecutive patients with T_3 or T_4 oral cancer treated about the same time with conventional fractions in air (63.00 Gy TD in 30 fractions in 38 days) where only 18 had locally controlled disease at 1 year, the results for control of the disease are significant at the 10% level ($\chi^2 = 2.7$) at 1 year. When the results are compared at 2 years (5/9 and 5/58), although the numbers are very small, the results are significant at less than the 1% level ($\chi^2 = 13.5$). A similar trend is seen when the results are compared with a retrospective series of 47 patients with T_3 mouth cancer (Sealy et al, 1982) treated with large fractions (36.00 Gy TD in six twice-weekly fractions in 18 days) where 11 patients were free of disease at 1 year ($\chi^2 = 3.9$ and 6% level of significance). The results also compare favourably with our past experience of irradiating patients with squamous carcinoma of the mouth in hyperbaric oxygen (45.00 Gy TD in nine twice-weekly fractions in 29 days) with T_3 (4–6 cm diameter), T_4 (greater than 6 cm diameter) or N_3 (fixed nodes) stage disease where one out of 13 patients was free of disease at 1 year. The difference is significant at less than the 5% level ($\chi^2 = 5.8$).

Nodal recurrence caused death in two patients in this series where the individual nodes were very large with diffuse disease in the neck and with estimated volumes of 39 cm^3 and 48 cm^3, respectively, whereas smaller nodes usually seem to have been controlled. In another two, nodal and primary recurrent disease was observed. Two of four patients who had disease involving bone, one with extensive destruction of the anterior mandibular arch, remain well with the primary growth area healed.

One remarkable feature of this method of treatment is the excellent patient tolerance to the prolonged hypothermic anaesthetic, which makes post-treatment care very easy.

DISCUSSION

We have formulated a theory for the clinical failure of hyperbaric oxygen radiotherapy and laid the groundwork for its application.

The clinical course of events so far supports the original thesis in that 27 of 29 patients in whom treatment was successfully completed, had complete regression of disease. These findings suggest that large primary growths in the mouth may have over 33% hypoxic cells and that large nodal metastases may have even more.

The very rapid regression rate seen with two hypothermic treatments, which seems to involve the whole tumour at once, is of interest since it does not have the same pattern as the classical centripetal regression of Coutard (1932). On the contrary, this is more in keeping with a large random and widespread tumour cell death at the initial treatment rather than that which might be seen with gradual reoxygenation. The slower rate of regression seen after one hypothermic treatment suggests that massive cell kill takes place with a second treatment and that a pattern of regression is induced with a single treatment more akin to that found with successful irradiation in air. Thus, it is possible that, even under the circumstances reported here, oxygen does not easily gain access to the tumour cells because of a poor and perhaps partially destroyed vasculature, as in a large, partially necrotic lymph node. This need only happen in one small area involving no more than about 10^7 cells for local recurrence to take place It is known that human tumour oxygen supply can vary greatly between regions of only a few millimetres in volume (Mueller-Klieser et al, 1981). Jung et al (1984) have recently shown that haemodilution increases tumour blood flow and the availability of oxygen to a rat tumour. After induction of the alpha adrenergic blockade, our patients received 2–3 l of fluid to maintain blood pressure which, thus, led to a fall in the haematocrit to about 30%. Moreover, our cardiac output studies show that a decrease did not occur due to the hypothermia, presumably due to a high cardiac output state induced by the fluid loading and alpha adrenergic blockade.

Others have found supporting evidence in a mouse tumour for the theory proposed here. Tozer et al (1984), in a search for anaesthetic agents to improve the results of irradiation in hyperbaric oxygen, found that a combination of ketamine and diazepam lowered the body temperature and improved the $TCD_{37/40}$ for a mouse mammary tumour in hyperbaric oxygen, but not in air. It is possible that the anaesthesia used in the early clinical experiences with irradiation, under hyperbaric oxygen, chlorpromazine and pentobarbitone sodium (Churchill-Davidson et al, 1957), acted in a similar manner.

The spinal cord has been rigorously avoided for those treatments given in hypothermic hyperbaric oxygen, but we are at present examining the late effects of single doses on pig spinal cord.

Although this approach is far from trivial and is labour intensive, it is no more so than major head and neck surgery. If a high success rate is maintained, it would be more cost effective than conventional methods of treatment with higher failure and all the attendant late care problems, quite apart from the overriding consideration of failure to cure.

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REFERENCES

ADAMS, G. E., 1978. Hypoxic cell sensitizers for radiotherapy *International Journal of Radiation Oncology, Biology, Physics, 4,* 135–141

BACHOFEN, M , GAGE, A & BACHOFEN, H , 1971. Vascular response to changes in blood oxygen tension under various blood flow rates. *American Journal of Physiology, 220,* 1786–1792.

BIGELOW, W. G., 1958 Hypothermia. *Surgery, 43,* 683–687

BIGELOW, W G., LINDSAY, W. K., HARRISON, R C , GORDON, R. A. & GREENWOOD, W. F., 1950. Oxygen transport and utilization in dogs at low body temperatures. *American Journal of Physiology, 160,* 125–137.

BLOCH, M., BLOOM, H J G , PENMAN, J. & WALSH, L , 1961 Irradiation of cerebral astrocytoma under whole-body hypothermia. *Lancet, ii,* 906–909.

CHANG, C. H., CONLEY, J. J. & HERBERT, C., 1973. Radiotherapy of advanced carcinoma of the oropharyngeal region under hyperbaric oxygenation. An interim report. *American Journal of Roentgenology, 17,* 509–516.

CHURCHILL-DAVIDSON, I., SANGER, C. & THOMLINSON, R. H., 1957. Oxygenation in radiotherapy. II Clinical application. *British Journal of Radiology, 30,* 406–422.

COUTARD, H., 1932. Roentgen therapy of epitheliomas of the tonsillar region, hypopharynx and larynx from 1920 to 1926 *American Journal of Roentgenology and Radium Therapy, 28,* 313–331.

CRABTREE, H G. & CRAMER, W., 1934. The action of radium on cancer cells. II Some factors determining the susceptibility of cancer cells to radium. III. Factors determining the susceptibility of cancer cells to gamma radiation. In *11th Scientific Report on the Investigations of the Imperial Cancer Research Fund* (Taylor and Francis, London), pp. 89–101, 103–117.

Denekamp, J., Fowler, J. F. & Dische, S., 1977. Letter to the Editor. The proportion of hypoxic cells in a human tumour. *International Journal of Radiation Oncology, Biology, Physics, 2*, 1227–1228.

Durand, R. E. & Biaglow, J. E., 1974. Modification of the radiation response of an *in vitro* tumour model by control of cellular respiration. *International Journal of Radiation Biology, 26*, 597–601.

Durand, R. E., Biaglow, J. E. & Sutherland, R. M., 1976. Hypoxic radiosensitizers and cellular respiration. *British Journal of Radiology, 49*, 567–568.

Ganong, W. F., 1983. *Review of Medical Physiology*, 11th edit. (Lange Medical Publications, Los Altos, California), 225 pp.

Hall, B. V., Hamilton, K. & Brues, A. M., 1952. Clarification of differences in radiosensitivity of tumours irradiated *in vitro* and *in vivo* on the basis of the effect of oxygen on radiosensitivity (Scientific Proceedings Abstract). *Cancer Research, 12*, 268.

Haynes, M. J. & Inch, W. R., 1976. Effect of metronidazole on the radiocurability and oxygenation of the C3HBA tumour. *Radiation Research, 68*, 184–189.

Henk, J. M., Kunkler, P. B. & Smith, C. W., 1977. Radiotherapy and hyperbaric oxygen in head and neck cancer. Final report of first controlled clinical trial. *Lancet, ii*, 101–103.

Henk, J. M. & Smith, C. W., 1977. Radiotherapy and hyperbaric oxygen in head and neck cancer. Interim report of second clinical trial. *Lancet, ii*, 104–105.

Hering, E. R., Blekkenhorst, G., Harrison, G. G., Morrell, D., Korrubel, J., Gregory, A., Phillips, J., Manca, V. & Sealy, R., 1986. Single-dose relative biological effectiveness and toxicity studies under conditions of hypothermia and hyperbaric oxygen. *British Journal of Radiology, 59*, 1099–1103.

Horvath, S. M. & Spurr, G. B., 1956. Effects of hypothermia on general metabolism. *National Academy of Sciences Washington Publications, 451*, 8.

Johnson, R. J. R., 1971. A comparison of the effect of hyperbaric oxygen and oxygen plus 5% CO$_2$ on tissue circulation and oxygenation. *Radiology, 98*, 177–181.

Johnson, R. J. R., Wiseman, N. & Wilson, L., 1972. The vascular response of tumour and normal tissue to hyperbaric oxygen. *Lahey Clinic Bulletin, 21*, 128–135.

Jung, C., Mueller-Klieser, W. & Vaupel, P., 1984. Tumour blood flow and oxygen availability during haemodilution. *Advances in Experimental Medicine and Biology, 180*, 281–291.

Milne, N., Hill, R. P. & Bush, R. S., 1973. Factors affecting hypoxic KHT tumour cells in mice breathing O$_2$, O$_2$+CO$_2$, or hyperbaric oxygen with or without anaesthesia. *Radiology, 106*, 663–671.

Morgan, R. L., 1967. Fast neutron therapy—clinical applications. In *Modern Trends in Radiotherapy*. Ed. by T. J. Deeley & C. A. P. Wood (Butterworths, London), pp. 171–186.

Moulder, J. E. & Rockwell, S., 1984. Hypoxic fractions of solid tumours experimental techniques, methods of analysis, and a survey of existing data. *International Journal of Radiation Oncology, Biology, Physics, 10*, 695–712.

Mueller-Klieser, W., Vaupel, P. & Manz, R., 1984. Effectiveness of respiratory hyperoxia, of normobaric and hyperbaric oxygen atmospheres in improving tumour oxygenation. *Advances in Experimental Medicine and Biology, 169*, 613–619.

Mueller-Klieser, W., Vaupel, P., Manz, R. & Schmidseder, R., 1981. Intracapillary oxyhaemoglobin saturation of malignant tumours in humans. *International Journal of Radiation Oncology, Biology, Physics, 7*, 1397–1404.

Novitzky, D., Boniaszczuk, J., Cooper, D. K. C., Isaacs, S., Rose, A. G., Smith, J. A., Uys, C. J., Barnard, C. N. & Frazer, R., 1984. Prediction of acute cardiac rejection using radionuclide techniques. *South African Medical Journal, 65*, 5–7.

Nunn, J. F., 1980. The effects of anaesthesia on respiration. In *General Anaesthesia*, 4th edit. Ed. by T. C. Gray, J. F. Nunn & J. E. Utting (Butterworths, London), Vol. 1, pp. 493–509.

Pallavicini, M. G. & Hill, R. P., 1983. Effect of tumour blood flow manipulations on radiation response. *International Journal of Radiation Oncology, Biology, Physics, 9*, 1321–1325.

Ross, D. N., 1954. Hypothermia: Part 2—Physiological observations during hypothermia. *Guy's Hospital Reports, 103*, 116–138.

Scott, O. C. A., 1957. A model system for examining the radiosensitivity of metabolizing layers of cells. *British Journal of Cancer, 11*, 130–136.

Sealy, R., 1979. Hyperbaric oxygen in radiotherapy. In *Advances in Medical Oncology, Research and Education. Basis for Cancer Therapy 2*. Ed. by M. Moore, (Pergamon Press, Oxford and New York), Vol. 6, pp. 223–233.

Sealy, R., Williams, A., Cridland, S., Stratford, M., Minchinton, A. & Hallet, C., 1982. A report on misonidazole in a randomized trial in locally advanced head and neck cancer. *International Journal of Radiation Oncology, Biology, Physics, 8*, 339–342.

Smith, T. D. & Richards, P., 1976. A simple kit for the preparation of ^{99m}Tc-labelled red blood cells. *Journal of Nuclear Medicine, 17*, 126–132.

Suit, H. D. & Maeda, M., 1967. Hyperbaric oxygen and radiobiology of a C$_3$H mouse mammary carcinoma. *Journal of the National Cancer Institute, 39*, 639–650.

Thomlinson, R. H. & Gray, L. H., 1955. The histological structure of some human lung cancers and the possible implications for radiotherapy. *British Journal of Cancer, 9*, 539–549.

Tozer, G. M., Penhaligon, M. & Nias, A. H. W., 1984. The use of ketamine plus diazepam anaesthesia to increase the radiosensitivity of a C$_3$H mouse mammary adenocarcinoma in hyperbaric oxygen. *British Journal of Radiology, 57*, 75–80.

UICC, 1978. *TNM Classification of Malignant Tumours*, 3rd edit. (UICC, Geneva).

Van Den Brenk, H. A. S., 1968. Hyperbaric oxygen in radiation therapy. *American Journal of Roentgenology, 102*, 8–26.

Whalen, R. E., Saltzman, H. A., Holloway, D. H., Jr, McIntosh, H. D., Sieker, H. O. & Brown, I. W., 1965. Cardiovascular and blood gas responses to hyperbaric oxygenation. *American Journal of Cardiology, 15*, 638–646.

Wright, S., 1971. *Samson Wright's Applied Physiology*, 12th edit. Ed. and revised by C. A. Keele & E. Neil (Oxford University Press, London), 204 pp.

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Single-dose relative biological effectiveness and toxicity studies under conditions of hypothermia and hyperbaric oxygen

By E. R. Hering, Ph.D., *G. Blekkenhorst, Ph.D., †G. G. Harrison, M.D., †D. Morrell, F.F.A. (S.A.),
J. Korrubel, H.T.S., †A. Gregory, H.T.S., *J. Phillips, M.S.R., †V. Manca, Ph.D. and
*R. Sealy, F.R.C.R.

Departments of Medical Physics, *Radiotherapy and †Anaesthetics, Groote Schuur Hospital and University of Cape Town, 7925 Observatory, South Africa

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ABSTRACT

An approach to using hyperbaric oxygen with radiation in a clinical situation has been described in the preceding paper in this issue. To ascertain whether there might be a change in the relative biological effectiveness of radiation on normal mammalian tissue treated under conditions of hypothermia and hyperbaric oxygen, the acute reaction to radiation of pig skin was studied. A single dose enhancement ratio at the erythema reaction level of 1.4 ± 0.08 was obtained when compared with irradiation at normal body temperature in air. We studied also a series of antioxidant enzymes in rat liver and lung after exposure to hypothermia and hyperbaric oxygen. Enzyme changes were such as to combat oxygen toxicity which might develop as a result of the pre-treatment.

In order to ascertain whether there is a change in the radiobiological effectiveness of radiation on normal mammalian tissue treated under hypothermia and hyperbaric oxygen (Sealy et al, 1986), we studied the acute radiation reaction on pig skin. This was chosen as our biological test system since it has been extensively used in RBE determinations (*e.g.* Fowler, 1981) and results can be extrapolated to the human with a high degree of confidence (Hall, 1978). In addition, drug administration regimes similar to those that were envisaged to be used on humans could be put into effect (Sealy et al, 1986).

Secondly, concern for the possibility of oxygen toxicity developing in patients as a result of the hypothermic hyperbaric oxygenation (Sealy et al, 1986) prompted a search for biochemical evidence of oxygen toxicity.

The biochemical probes chosen were the activities of rat lung and rat liver superoxide dismutase, catalase, glutathione reductase, glutathione peroxidase, and also glucose-6-phosphate dehydrogenase, since the activity of this enzyme has been shown to be increased on exposure to hyperoxia (Tierney et al, 1973). Glutathione levels were also investigated.

METHODS

Pigs

Pigs of the Large White/Landrace cross variety were used, weighing between 50 kg and 60 kg. In total, nine pigs (three sets of three litter mates) were used in the investigation. Every pig was irradiated to one or more dose levels under each of the following conditions:

(a) in air at normal body temperature (range 34.5–36.5°C);
(b) in hyperbaric oxygen (3 atmospheres absolute) at normal body temperature (range 34.5–36.5°C);
(c) in air at hypothermic body temperature (range 28–31°C);
(d) in hyperbaric oxygen at a hypothermic body temperature (range 28–31°C).

Anaesthesia, cooling and profound vasodilatation in the pigs was achieved in essentially the same manner as that described by Sealy et al (1986) for patients. Experimental animals, to which balanced salt solution and drugs were administered via jugular venous cannulation, were anaesthetised by Alfathesin (alphazalone and alphadalone compound, Glaxo) or Hypnomidate (etomidate, Janssen) by continuous infusion, curarised with Alloferin (alcuronium chloride, Roche) and intubated, ventilated by means of a Vickers fluid logic ventilator and subjected to alpha-adrenergic blockade with Regitine (phentolamine, Ciba-Geigy). Hypothermia was induced by surface cooling with ice packs, care being taken not to cover the areas to be irradiated. Rewarming was achieved by immersion of the animal in water at approximately 40°C. The temperature of the animal was measured on the skin near the irradiated area and in the oesophagus using thermistor probes with a Vickers thermometer.

Irradiation of pig skin. Irradiations were carried out inside a single-patient hyperbaric oxygen chamber (Vickers Mark IV). Eight fields, each 5 cm × 5 cm, were marked by tattooing, four on the right hindquarter and four on the right forequarter of each pig with at least 3 cm between each field. Each field was treated to a dose ranging from 15 Gy to 29 Gy on the surface of the skin

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Address for correspondence: E. R. Hering, Department of Medical Physics, Groote Schuur Hospital, 7925 Observatory, Cape Town, South Africa

TABLE I

DEGREE OF RADIATION REACTION OF PIG SKIN

Score	Reaction
0.5	No reaction
1.0	Faint erythema
1.5	Erythema
2.0	Marked erythema
2.5	Moist desquamation of less than half of the irradiated area
3.0	Moist desquamation of more than half of the irradiated area

Eight-megavolt X rays from a Philips SL 75/20 linear accelerator were used with 2 cm tissue-equivalent polystyrene build-up. In order to prevent any hypoxia occurring due to pressure, the polystyrene plate was suspended immediately above the surface of the skin. The animals were irradiated with a vertical beam whilst lying on the left side inside the hyperbaric oxygen cylinder. The doses were measured using a Baldwin-Farmer ionisation chamber and LiF thermoluminescent dosemeters. The dose rate at the skin surface was 1.736 Gy/min.

Skin scoring. The method of estimating the skin reactions was that of visual observations carried out on Mondays, Wednesdays and Fridays by three to five observers who were unaware of how each area had been irradiated. An arbitrary scale was adopted based on that used by Fowler et al (1963) (Table I).

Rats

Male Long-Evans rats, weighing between 250 g and 270 g, were used. Rats were maintained on a standard laboratory diet and allowed food and water *ad libitum*. Animals were divided randomly into four groups of six rats. One group of rats served as controls and received no treatment. The second group of rats (the "hyperbaric" group) was exposed for 4 h to 100% oxygen at 303 kPa. The third group was treated intraperitoneally with 70 mg/kg sodium pentobarbital (Sagatal, May and Baker) to induce hypothermia (Pallavicini & Hill, 1983). The fourth group of rats (the hypothermic hyperbaric oxygen group) received 70 mg/kg sodium pentobarbital intraperitoneally, immediately following which they were placed in 100% oxygen at 303 kPa for 4 h. Exposures to hyperbaric oxygen were conducted in a Vickers Mark IV single-patient hyperbaric oxygen chamber. Temperature was measured in both the hypothermic group and the hypothermic hyperbaric oxygen group with an Electrolaboratoriet monitor by means of thermocouples placed under the skin in the abdominal area. The animals in the hypothermic group and in the hypothermic hyperbaric oxygen group were placed in cages positioned on plastic bags containing melting ice immediately after injection of the sodium pentobarbital. It was found that the temperature in both groups treated with sodium pentobarbital decreased from 36°C to a minimum of 29°C.

Tissue preparation and measurement of biochemical parameters. Rats were sacrificed by cervical dislocation 24 h after commencement of the treatments above, the lungs and livers being removed and used immediately. Cytosol Cu/Zn superoxide dismutase was extracted by the method of McCord and Fridovich (1969) as modified by Sykes et al (1978), and assayed by following the auto-oxidation of epinephrine to adrenochrome (Misra & Fridovich, 1972). Determination of glucose-6-phosphate dehydrogenase was by the method of Löhr and Waller (1963). Catalase was determined by the method of Holmes and Masters (1970), glutathione by the method of Saville (1958), glutathione peroxidase by the method of Lawrence and Burk (1976), glutathione reductase by the method of Worthington and Rosemeyer (1974) and protein as described by Lowry et al (1951).

The significance of differences between mean values for the groups was assessed by Student's t-test.

RESULTS

Figure 1 shows the variation of the average skin reaction with time for a single pig irradiated to 23 Gy

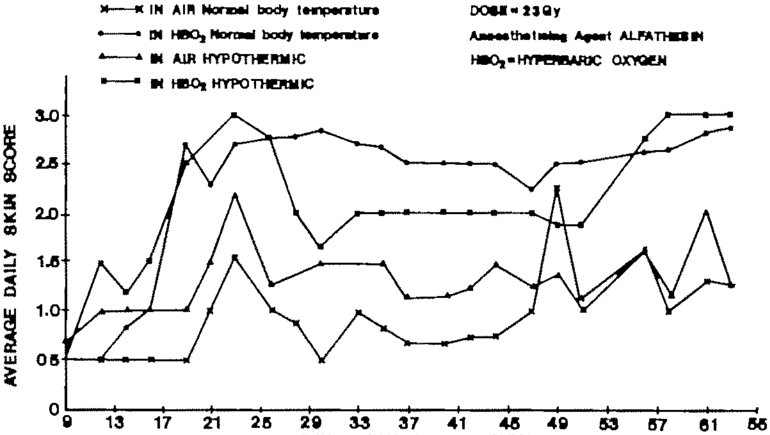

FIG. 1.

Acute radiation responses for pig skin under the four conditions. End-point represents the average score for all scorers for two fields. Note the increased reaction for those areas irradiated in oxygen and the curve suggesting a triphasic response.

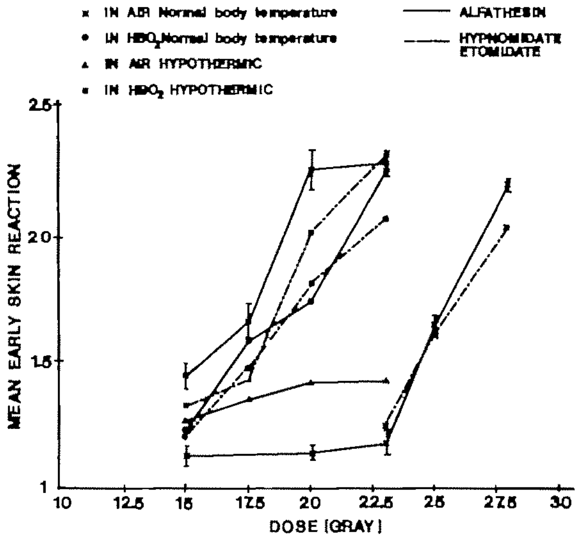

FIG 2

The mean early skin reaction for various doses in nine pigs. Data points are given together with standard errors of the means. Not all error bars are shown in order to preserve clarity.

under the various conditions. In general, an early wave of reaction reaching a peak at about 25 days after irradiation was observed, followed by a slight decrease in reaction to a more or less constant, slightly lower level. At about 50 days after irradiation the reaction increased again in intensity. This reaction pattern is similar to that observed by Fowler et al (1963).

The dose–response curves (Fig. 2) were obtained by determining the average skin reaction between the time when the reaction first became apparent (lower limit) and when it started to increase to the second peak (upper limit). This is the early reaction stage referred to by Hall (1978). The size of the animals and maintenance limited us to this region.

The shape of the dose–response curves obtained (Fig. 2) resemble those of Fowler et al (1963). From these curves the values for the radiobiological effectiveness relative to the treatment at normal body temperature in air (RBE) were determined, and are listed in Table II. The radiobiological effectiveness was determined at the 1.5 reaction level because patients would not be treated to skin doses resulting in a greater level of damage

It was noted that the skin damage is increased only slightly under hypothermic conditions in air compared with normal body temperature in air, whereas there was a significant increase in effect for hypothermic/normothermic treatments in hyperbaric oxygen (Fig. 2) compared with irradiation in air.

Results of the hepatic and pulmonary measurements in rats are given in Tables III and IV.

TABLE II

STUDY OF PIG SKIN REACTION USING HYPOTHERMIA IN CONJUNCTION WITH HYPERBARIC OXYGEN

Anaesthetising agent	Conditions at irradiation	Enhancement ratio at 1.5 reaction level
Alfathesin	In Air Warm	Standard
	In HBO$_2$ Warm	1.4
	In HBO$_2$ Cold	1.5
Hypnomidate	In Air Warm	Standard
	In HBO$_2$ Warm	1.4
	In HBO$_2$ Cold	1.4

HBO$_2$ hyperbaric oxygen.
An error estimate of about ±0.08 on the values for the enhancement ratio was obtained by a simple "envelope of errors" analysis on the dose–response curves.

TABLE III

THE EFFECT OF HYPERBARIA, HYPOTHERMIA AND HYPERBARIC HYPOTHERMIA ON BIOCHEMICAL PARAMETERS CHOSEN AS PROBES FOR OXYGEN TOXICITY IN RAT LIVER THE MEAN RESULTS ±SEM FOR DETERMINATIONS IN SIX ANIMALS ARE GIVEN

Parameter	Controls	100% O$_2$ at 303 kPa for 4 h	70 mg/kg sodium pentobarbital	70 mg/kg sodium pentobarbital, 100% O$_2$ at 303 kPa for 4 h
Superoxide dismutase (units/mg protein)	1570±245	1779±223	1674±505	5000±879§
Catalase (μmol H_2O_2 degraded/min/mg protein)	135.0±8.7	106.6±14.8	119.6±29.9	178.2±13.4*
Glutathione (nmol glutathione/mg protein)	167.7±6.5	218.0±24.9	161.0±25.8	244.5±28.8*
Glutathione peroxidase (nmol NADPH oxidised/min/mg protein)	3.8±0.6	6.0± 0.9	7.6± 1.6	11.3± 1.5§
Glutathione reductase (nmol NADPH oxidised/min/mg protein)	48.0±1.7	69.7±6.2†	101.4±8.9§	65.9±3.8‡
Glucose-6-phosphate dehydrogenase (nmol NADP reduced/min/mg protein)	17.7±1.3	31.0±5.0*	27.7±3.9	20.3±2.9

Significantly different from control: *$p < 0.05$; †$p < 0.01$; ‡$p < 0.002$, §$p < 0.001$

TABLE IV

THE EFFECT OF HYPERBARIA, HYPOTHERMIA AND HYPERBARIC HYPOTHERMIA ON BIOCHEMICAL PARAMETERS CHOSEN AS PROBES FOR OXYGEN TOXICITY IN RAT LUNG. THE MEAN RESULTS ±SEM FOR DETERMINATIONS IN SIX ANIMALS ARE GIVEN

Parameter	Controls	100% O_2 at 303 kPa for 4 h	70 mg/kg sodium pentobarbital	70 mg/kg sodium pentobarbital, 100% O_2 at 303 kPa for 4 h
Superoxide dismutase (units/mg protein)	149±11	131±25	381±111.5‡	474±220*
Catalase (μmol H_2O_2 degraded/min/mg protein)	19.9±0.5	29.7±2.6‡	17.5±4.9	39.9±5.0‡
Glutathione (nmol glutathione/mg protein)	282.7±8.5	332.0±14.3†	105.1±15.4§	165.8±11.4§
Glutathione peroxidase (nmol NADPH oxidised/min/mg protein)	5.5±0.4	7.8±1.1	12.2±2.6*	11.3±1.9†
Glutathione reductase (nmol NADPH oxidised/min/mg protein)	8.0±0.3	12.6±0.9§	12.1±1.4*	9.1±1.6
Glucose-6-phosphate dehydrogenase (nmol NADP reduced/min/mg protein)	11.6±0.7	18.0±1.4‡	17.9±2.2*	14.6±2.5

Significantly different from control $^*p < 0.05$; $^†p < 0.02$, $^‡p < 0.01$; $^§p < 0.001$.

DISCUSSION

The pig skin studies have shown that, when irradiated in hyperbaric oxygen, the skin reaction was always greater than when treated in air, irrespective of body temperature. The RBE values listed in Table II indicate that, while there is an increased effect in those areas irradiated under conditions of hypothermic hyperbaric oxygenation compared with normal temperature in air, the differences were not statistically significant when compared with those irradiated at normal temperature in hyperbaric oxygen.

It has been demonstrated by Stewart et al (1982) that normal rodent skin is mildly hypoxic. Our findings indicate that, even under the influence of alpha-adrenergic blockade in air, there are some hypoxic cells in normal pig skin and that the protective effect of the hypoxia is partially reversed by hypothermia alone, but more efficiently by hyperbaric oxygenation. The modest effect of hypothermic hyperbaric oxygenation compared with hyperbaric oxygenation at normal temperatures could be explained by the latter overcoming the protective effect of nearly all the hypoxic cells. If our hypothesis is correct, a much greater margin might be expected if large tumours were irradiated, since the proportion of hypoxic cells would be expected to be much greater than in normal skin or smaller tumours.

The lung and liver play major roles in the defence of the body against oxygen toxicity. In the clinical situation, where patients are treated radiotherapeutically under conditions of hyperbaric oxygenation and hypothermia, the duration of the hyperbaric oxygen is about 40 min (Sealy et al, 1986). The antioxidant enzymes are inducible (Tierney et al, 1973; Crapo and Tierney, 1974; Kimball et al, 1976; Rister & Baehner, 1976; Frank et al, 1978) and can provide protection against hyperoxic challenges. In support of this, Deneke and Fanburg (1982) reported that significant increases in the activities of superoxide dismutase, glucose-6-phosphate dehydrogenase, glutathione peroxidase and reductase and, in some instances, catalase occur within 24–48 h in young animals exposed to 100% oxygen. This enabled the animals to resist the toxic effects of 100% oxygen (Frank et al, 1978). It can, thus, be expected that if acute oxygen toxicity in rats was to develop as a result of hypothermia or hypothermic hyperbaric oxygenation, the activities of these enzymes would, in fact, not be increased

Superoxide dismutase was not induced in the lung by hyperbaric oxygen alone, but was increased almost twofold after sodium pentobarbital and threefold after the combination of pentobarbital and hyperbaric oxygen. We noted also a more than threefold increase in hepatic superoxide dismutase activity following sodium pentobarbital-induced hypothermia and hyperbaric oxygen. These increases in superoxide dismutase activity may afford protection against the increase in free superoxide radicals that might be produced under these conditions.

Glutathione reductase in the lung was induced in response to hyperbaric oxygenation, thus implying a continued supply of reduced glutathione which protects cells under oxidative stress by scavenging free radicals and peroxides (Meister & Tate, 1976). The observed depletion of pulmonary glutathione after sodium pentobarbital or hyperbaric oxygen together with sodium pentobarbital may be partly due to the increase in the activity of glutathione peroxidase in both of these situations.

Increases in activity of antioxidant enzymes have generally only been shown to occur following several days of exposure to hyperoxia (Crapo & Tierney, 1974, Kimball et al, 1976; Rister & Baehner, 1976; Frank et al, 1978). The observed changes in this study after a 4 h exposure to hypothermia and hyperbaric oxygen were, in general, of such a nature that potential hepatic and pulmonary oxygen toxicity or the effects thereof would be combated. Our biochemical evidence is such that oxygen toxicity will probably not develop during the course of or during hypothermic hyperbaric oxygen irradiation of patients.

Acknowledgments

Thanks are due to the Chief Medical Superintendent of Groote Schuur Hospital for permission to publish this work. The work was supported by the National Cancer Association of South Africa, the Groote Schuur Hospital Board, the University of Cape Town, the Radiotherapy Department Research Fund, and the Anglo-American and De Beers Anaesthetic Research Fund. We are grateful to Brian Sassman and Harold Stuurman of the Department of Anaesthetics Laboratory for their assistance. The concentrated formulation of etomidate (not generally available) was provided gratis by Janssen Pharmaceutica of Randburg, South Africa.

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REFERENCES

Crapo, J. D. & Tierney, D. F., 1974. Superoxide dismutase and pulmonary oxygen toxicity. *American Journal of Physiology, 226*, 1401–1407.

Deneke, S. M. & Fanburg, B. L., 1982. Oxygen toxicity of the lung: an update. *British Journal of Anaesthesia, 54*, 737–749.

Fowler, J. F., 1981. Radiobiological principles. In *Medical Physics Handbook 8. Nuclear Particles in Cancer Treatment*. Ed. by J. M. A. Lenihan (Adam Hilger, Bristol), pp. 100–125.

Fowler, J. F., Morgan, R. L., Silvester, J. A., Bewley, D. K. & Turner, B. A., 1963. Experiments with fractionated X-ray treatment of the skin of pigs. 1—Fractionation up to 28 days. *British Journal of Radiology, 36*, 188–196.

Frank, L., Bucher, J. R. & Roberts, R. J., 1978. Oxygen toxicity in neonatal and adult animals of various species. *Journal of Applied Physiology, 45*, 699–704.

Hall, E. J., 1978. Dose–response relationships for normal tissues. In *Radiobiology for the Radiologist* (Harper and Row, London), pp. 63–78.

Holmes, R. S. & Masters, C. J., 1970. Epigenetic interconversions of the multiple forms of mouse liver catalase. *FEBS Letters, 11*, 45–48.

Kimball, R. E., Reddy, K., Peirce, T. H., Schwartz, L. W., Mustafa, M. G. & Cross, C. E., 1976. Oxygen toxicity: augmentation of anti-oxidant defence mechanisms in rat lung. *American Journal of Physiology, 230*, 1425–1431.

Lawrence, R. A. & Burk, R. F., 1976. Glutathione peroxidase activity in selenium-deficient rat liver. *Biochemical and Bio-physical Research Communications, 71*, 952–958.

Löhr, G. W. & Waller, H. D., 1963. Glucose-6-phosphate dehydrogenase. In *Methods of Enzymatic Analysis*. Ed. by H. U. Bergmeyer (Academic Press, New York), Vol. 2, pp. 636–643.

Lowry, O. H., Rosebrough, N. J., Farr, A. L. & Randall, R. J., 1951. Protein measurement with the Folin phenol reagent. *Journal of Biological Chemistry, 193*, 265–275.

McCord, J. M. & Fridovich, I., 1969. Superoxide dismutase. An enzymic function for erythrocuprein (haemocuprein). *Journal of Biological Chemistry, 244*, 6049–6055.

Meister, A. & Tate, S. S., 1976. Glutathione and related γ-glutamyl compounds: biosynthesis and utilization. *Annual Reviews of Biochemistry, 45*, 559–604.

Misra, H. P. & Fridovich, I., 1972. The rôle of superoxide anion in the auto-oxidation of epinephrine and a simple assay for superoxide dismutase. *Journal of Biological Chemistry, 247*, 3170–3175.

Pallavicini, M. G. & Hill, R. P., 1983. Effect of tumour blood flow manipulations on radiation response. *International Journal of Radiation Oncology, Biology, Physics, 9*, 1321–1325.

Rister, M. & Baehner, R. L., 1976. The alteration of superoxide dismutase, catalase, glutathione peroxidase and NAD(P)H cytochrome c reductase in guinea pig polymorphonuclear leukocytes and alveolar macrophages during hyperoxia. *Journal of Clinical Investigation, 58*, 1174–1184.

Saville, B., 1958. A scheme for the colorimetric determination of microgram amounts of thiols. *Analyst, 83*, 670–672.

Sealy, R., Harrison, G. G., Morrell, D., Korrubel, J., Gregory, A., Barry, L., Blekkenhorst, G., Hering, E. R., Fataar, A. B. & Boniaszczuk, J., 1986. A feasibility study of a new approach to clinical radiosensitisation: hypothermia and hyperbaric oxygen in combination with pharmacological vasodilatation. *British Journal of Radiology, 59*, 1093–1098.

Stewart, F. A., Denekamp, J. & Randhawa, V. S., 1982. Skin sensitization by misonidazole: a demonstration of uniform mild hypoxia. *British Journal of Cancer, 45*, 869–877.

Sykes, J. A., McCormack, F. X., Jr & O'Brien, T. J., 1978. A preliminary study of the superoxide dismutase content of some human tumours. *Cancer Research, 38*, 2759–2762.

Tierney, D. F., Ayers, L., Herzog, S. & Yang, J., 1973. Pentose pathway and production of reduced nicotinamide adenine dinucleotide phosphate. A mechanism that may protect lungs from oxidants. *American Review of Respiratory Disease, 108*, 1348–1351.

Worthington, D. J. & Rosemeyer, M. A., 1974. Human glutathione reductase: purification of the crystalline enzyme from erythrocytes. *European Journal of Biochemistry, 48*, 167–177.

Book reviews

Radionuclides in Haematology (Vol. 14 in "Methods in Haematology"). Ed. by S. M. Lewis and R. J. Bayly, pp viii+262+index, 1986 (Churchill Livingstone, Edinburgh), £32.00.
ISBN 0-443-03191-6

This volume (No 14 in the ongoing series "Methods in Haematology") is devoted to the use of radionuclides as a diagnostic tool in haematological practice. It sets out to be a comprehensive survey of the various methods currently used, and each chapter is designed as a critical, in-depth review of a particular technique or topic. There are 12 chapters, each by a different author or group of authors who are experienced in the methods they discuss.

The first two chapters provide some basic physics, a down-to-earth discussion of some prerequisites for the use of radionuclides and a survey of instrumentation and methods for their detection and counting. Chapter 3 describes *in-vitro* methods for radioassay and quantification of substances of importance in the diagnosis of haematological disorders. Whole-cell labelling and tracking is the topic for Chapter 4. Next, the complex problem of protein labelling is considered and various applications of protein tracers illustrated. A useful practical appendix on experimental methods for making radioiodine-tagged proteins concludes this chapter. Chapter 6 deals briefly with autoradiography at both light and electron microscope levels and again provides practical guidance by way of schedules and formulae. The book then moves on to deal with two applications requiring expensive instrumentation and expert personnel, namely the imaging and quantitative scanning of radioactivity in body organs and structures, and a short chapter on whole-body counting. The last four chapters review specific fields where radioactive tracers have been extensively used in haematology: absorption and excretion, blood volume, plasma clearance and blood-cell survival.

As is inevitable in a multi-author publication, the presentation quality and content selection of chapters varies, but, overall, I found this an interesting and helpful book. The high standards achieved by this series are certainly maintained. In their preface the editors indicate that the book is directed primarily at the haematologist wishing "to learn something of the basic principles of the application of radionuclides . . . and to be brought up to date on recent developments". I believe they have achieved their objective admirably.

JOHN R. K. SAVAGE

Cancer Metastasis: Experimental and Clinical Strategies. Progress in Clinical and Biological Research, Vol. 212. Ed. by D. R. Welch, B. K. Bhyan and L. A. Liotta, pp 352, 1986 (Alan R. Liss Inc., New York), £39.
ISBN 0-8451-5062-6

"One of the major causes of treatment failure in the cancer patient is the formation of resistant metastatic tumor cells. At the present time, there is no single clinically useful agent whose major therapeutic activity could be described as antimetastatic." So says the dust jacket of this 212th volume in the series "Progress in Clinical and Biological Research". The 19 chapters form the proceedings of a symposium held in Kalamazoo, Michigan, in September 1985. The organisers are to be congratulated for publishing the book just 7 months later. Sadly, no such rapid solution has been offered to the problem of metastasis.

Hellman started looking for antimetastatic drugs 20 years ago and "with the first compound in the first experiment in the first screen, we completely abolished the metastases without any immediately obvious effects on the growth of the primary implant". This was using the Lewis lung carcinoma as an experimental tumour model. "If it was that easy, we felt it was highly likely that many other compounds would do the same. We were wrong." Indeed, razoxane has not fulfilled that early promise in clinical use.

Perhaps the wrong model system had been used. In this book, there are several chapters devoted to the choice of model. But perhaps the best contribution is from Dorothy Glaves at Roswell Park Memorial Institute where Leonard Weiss has researched this problem for many years. "There are few reliable quantitative estimates of circulating human cancer cells so that the relevance of experimental systems to human cancer is still uncertain." There is not even evidence for a role of oncogenes in this field. The only comfort to be derived from this book is that no obvious stone has been left unturned, and several useful leads are suggested.

A. H. W. NIAS

1986, *The British Journal of Radiology*, *59*, 1105–1107 NOVEMBER 1986

The evaluation of radioiodine therapy for thyroid patients using a fixed-dose regime

By Guy E. Ratcliffe, M.B., M.R.C.P., Ignac Fogelman, B.Sc., M.D., M.R.C.P. and Michael N. Maisey, B.Sc., M.D., F.R.C.P.

United Medical and Dental Schools of Guy's and St Thomas's Hospital, Department of Nuclear Medicine and Endocrinology, Guy's Hospital, London SE1

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ABSTRACT

Ninety-six patients with toxic diffuse goitre (Graves' disease) in whom rapid control of disease was necessary were treated with an "ablative" dose of 550 MBq of radioiodine (^{131}I) with the intention of inducing hypothyroidism Outcome was established in 93 cases (mean follow-up 37 months), 45 patients (48%) becoming hypothyroid, 30 (32%) remaining euthyroid and 18 (19%) with persistent thyrotoxicosis requiring further ^{131}I therapy It is thus apparent that a fixed dose of 550 MBq ^{131}I cannot be considered ablative, with less than 50% of patients developing hypothyroidism.

The use of radioiodine (^{131}I), for the treatment of diffuse toxic goitre (Graves' disease) is well established. Ideally, one would hope that all patients would remain euthyroid following treatment At the present time, this goal appears unattainable as the incidence of hypothyroidism is in the range of 30–70% 10 years after ^{131}I therapy and this is relatively independent of administered dose (Glennon et al, 1972).

Wise et al (1975) reported that a fixed dose of 15 mCi (550 MBq) of ^{131}I resulted in the rapid control of hyperthyroidism in most patients with Graves' disease and was associated with a high (92%) early occurrence of hypothyroidism. This approach, being relatively simple and inexpensive, has been advocated for the treatment of all patients with hyperthyroidism (Kendall-Taylor et al, 1984) However, the aim should be to cure disease and not to substitute another condition which is simpler to treat. Nevertheless, there are some thyrotoxic patients for whom rapid and permanent control of disease is desirable and for whom development of early hypothyroidism is, therefore, acceptable. Patients who fall into this category include those with cardiac disease (both heart failure and atrial fibrillation) or severe and complicated non-thyroid disease, elderly and infirm patients, patients who have had surgery for hyperthyroidism, and possibly some patients with chronic mental illness. This study was undertaken to assess the success of the simple regime recommended by Wise et al (1975) as applied to patients with complicated Graves' disease

PATIENTS AND METHODS

Patients

Patients were referred to the thyroid clinic at Guy's Hospital to be considered for ^{131}I therapy between 1974 and 1982 This study includes only those who had a clinical indication for rapid control and for whom it was felt that the high probability of subsequent hypothyroidism justified the use of a high ^{131}I dose to achieve early permanent control. All the patients were hyperthyroid by the usual clinical and biochemical criteria, including elevated total triiodothyronine and thyroxine measured by radioimmunoassay (T3 RIA and T4 RIA, Radiochemical Centre Amersham). Before ^{131}I therapy, a radionuclide scan was performed 20 min after the injection of 180 MBq of ^{99}Tc^{m} pertechnetate, using a gamma camera fitted with a pinhole or long parallel-hole special thyroid collimator Only patients with evidence of a diffuse uptake confirming Graves' disease rather than Plummer's disease were included in this review.

Radioiodine therapy

Treatment with 550 MBq ^{131}I consisted of a single, oral dose of sodium iodide. When antithyroid drugs had been prescribed prior to referral they were stopped at least 3 days before treatment with ^{131}I and were usually restarted 48 h later, and then discontinued as the patient became euthyroid or hypothyroid. The likely consequences of the treatment were fully explained to all patients and relatives, the usual precautions to prevent unnecessary irradiation of the public were instituted and all patients were followed up carefully with regular thyroid function tests, usually at 6 weeks, 3 months, 6 months, 9 months and 1 year, and then annually. Patients who became hypothyroid were in most cases then discharged to the care of their own general practitioner, after stabilisation on thyroxine.

RESULTS

Ninety-six patients were included, having met the criteria of complicated Graves' disease in whom early rapid control was clinically indicated (Table I). Follow-up information is available for 93; two patients were lost to follow-up and one died of non-thyroidal illness

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Address for reprints. Professor M. N. Maisey, Department of Radiological Sciences, Guy's Hospital, London SE1

TABLE I

INDICATIONS FOR ABLATIVE THERAPY WITH ^{131}I

Indications	No. of patients
Elderly patients	12
Poor drug compliance	5
Associated psychiatric disease	3
Associated non-thyroid cardiac disease	10
Cardiac complication of thyroid disease	
Atrial fibrillation alone	18
Cardiac failure alone	16
Cardiac failure with atrial fibrillation	11
Poor control of hyperthyroidism	21

with inadequate information as to the thyroid status at the time of death.

The mean age of the group was 61.7 (range 28–86) years, and the female : male ratio was 4.3 : 1

Sixteen patients had had previous thyroid surgery between 3 months and 32 years before the radioiodine treatment.

Seventy-two patients had been receiving antithyroid drugs (carbimazole or propylthiouracil) for more than 3 weeks before treatment but all had stopped taking these 3 days before receiving ^{131}I Eight patients had had either no treatment or only beta-blocker therapy before receiving ^{131}I.

A summary of the results is shown in Fig. 1. Of the 93 patients, 48% were hypothyroid on replacement thyroxine at the time of follow-up review 1–9 years later (average of 37 months). The mean time of onset of hypothyroidism was 6.4 months. Thirty-two per cent remained euthyroid at the follow-up review, although eight additional patients were initially euthyroid at 6 months but subsequently relapsed during the next 6 months.

Ten patients remained hyperthyroid 6 months after treatment. Thus there were 18 patients (19%) remaining hyperthyroid 6 months after ^{131}I therapy and, because of the initial plan of treatment, they were treated with a second 550 MBq dose of ^{131}I. The one exception was a patient who refused further ^{131}I therapy and who has subsequently been maintained on antithyroid drugs. Of the 17 patients treated again, 10 became hypothyroid by the time of review and seven have remained euthyroid.

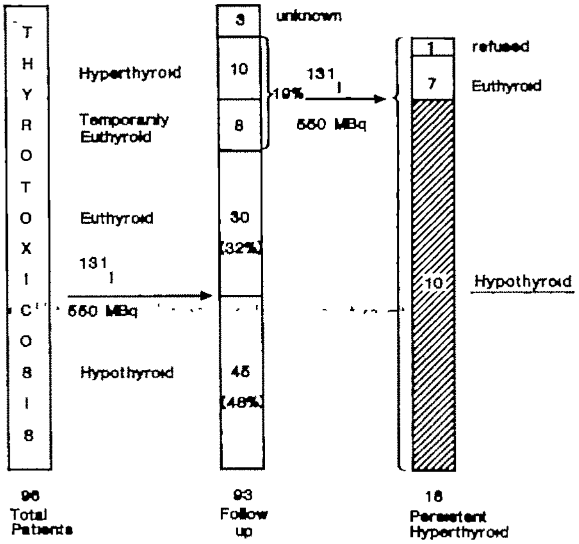

FIG 1

Results of 1–9 year follow-up.

There were no patients who required more than two doses of ^{131}I in this series.

Table II compares the subgroup of patients in this series who were pre-treated with antithyroid drugs with those who did not receive antithyroid drugs. The most obvious finding was that whereas 17 of 70 patients receiving antithyroid drugs required further ^{131}I treatment, none of those who were not receiving them required further therapy.

DISCUSSION

In this study we have found that, even when an "ablative" dose of 550 MBq of ^{131}I was given for complicated thyrotoxicosis where rapid definitive therapy was clinically desirable, in 19% of cases disease persisted at 6 months and less than half the patients (48%) became hypothyroid. This is in contrast to the findings of Wise et al (1975) who found that 92% of their patients were hypothyroid and 8% euthyroid at 6 months, none remaining hyperthyroid. More recently, Kendall-Taylor et al (1984) found an incidence of hypothyroidism of 58% at 6 months and 64% at 1 year,

TABLE II

A COMPARISON OF SUBGROUPS OF PATIENTS RECEIVING ^{131}I TREATMENT

	No of patients				
	Total	Hypothyroid	Euthyroid	Requiring further therapy	Lost to follow-up
Pre-treated with antithyroid drugs	72	32	21	17	2
No antithyroid drugs	8	2	6	0	

only 5.6% failing to become euthyroid within 1 year. On the other hand, Scott et al (1984), using 600 MBq, induced hypothyroidism in only 48% of patients within 6 months, a figure identical with ours. There are a number of possible reasons for these discrepancies. Our patients were selected because of the need for rapid control of their thyrotoxicosis and it is therefore possible that, as a group, they exhibit greater resistance to radiation therapy for genetic, environmental, dietary or other reasons not immediately apparent. None of the patients who did not receive antithyroid drug therapy before ^{131}I treatment required a second dose of ^{131}I to control their hyperthyroidism. While the numbers are small, it seems probable that carbimazole exerts a radioprotective effect, either directly or by alteration of the iodine kinetics (Crooks et al, 1960). Thus, higher doses of ^{131}I may be necessary for patients receiving antithyroid drugs as withdrawal of drugs increases the risk of recurrence of disease as well as the risk of post-therapy thyrotoxic crisis due to the sudden release of thyroid hormones Furthermore, while the administered dose of ^{131}I may be the same as in previous studies, it does not follow that the dose to the thyroid is the same. This depends on gland size, uptake, turnover and distribution of radioactivity within the gland itself. For example, it has been shown that per mCi dose the actual dose in cGy delivered may vary by a factor of 10 between patients (Becker & Hurley, 1982).

It would seem attractive to advocate using a simple regime, such as 550 MBq of ^{131}I, for the treatment of patients with complicated thyrotoxicosis as the time and effort (and consequently expense) spent trying to improve the radiation dosimetry is probably not justifiable when rapid and definitive control is required. However, it is clear from the present study that such a dose cannot be considered ablative, and a significant number of patients have had to receive further treatment with ^{131}I because of persistent thyrotoxicosis. Further prolonged follow-up is necessary in patients who are not rendered hypothyroid.

REFERENCES

BECKER, D. V. & HURLEY, J. R., 1982. Current status of radioiodine (131I) treatment of hyperthyroidism. In *Nuclear Medicine Annual* Ed. by L. M. Freeman & H S Weissman (Raven Press, New York), pp 265–290.

CROOKS, J., BUCHANON, T. W , WAYNE, E. J. & MACDONALD, E., 1960. Effect of pretreatment with methylthiouracil on results of I131 therapy. *British Medical Journal, i,* 151–154

GLENNON, J A , GORDON, E. S. & SAWIN, C. J , 1972 Hypothyroidism after low dose I131 treatment of hyperthyroidism. *Annals of Internal Medicine, 76,* 721–723

KENDALL-TAYLOR, P., KEIR, M J & ROSS, W. M., 1984 Ablative radioiodine therapy for hyperthyroidism long term follow up study *British Medical Journal, 289,* 361–363.

SCOTT, G. R , FORFAR, J. C. & TOFT, A. D., 1984. Graves' disease and atrial fibrillation· the case for even higher doses of therapeutic iodine 131. *British Medical Journal, 289,* 399–400

WISE, P. H., BURNET, R. B., AHMAD, A. & HARDING, P. E., 1975. Intentional radioiodine ablation in Graves' disease. *Lancet,* 1231–1232.

Book reviews

Radiology of the Spine—Tumors. Ed. by L. Jeanmart, pp. 118, 1986 (Springer-Verlag, Berlin), DM 138.
ISBN 3-540-15326-8 (Berlin)
0-387-15326-8 (New York)

This monograph is the latest in the series *Radiology of the Spine*, edited by Dr Louis Jeanmart with contributions from European authors, apart from Dr Harwood-Nash, Hospital for Sick Children, Toronto.

The chapters are divided into technical aspects, tumours of bone, spinal cord, neurinomas, haemangiomas and metastases, with more general contributions on paediatric problems and radionuclide studies. A criticism of a multi-author text is that there may be overlap and repetition, but this is not the case here. There is, however, considerable disparity in the contents of the chapters, notably "Primary tumors of the osseous spine" (Stienon and Jeanmart), where there is no bibliography and only very brief mention of the rare, but important, osteoid osteoma. This compares with "Metastatic disease of the spine. contributions of bone scintigraphy" (Frühling) which presents a personal series in considerable detail. The remaining chapters follow the style of plain radiographs, myelography, computed tomography, CTM, angiography and brief mention of magnetic resonance imaging. The only personal criticism of the contents is the recommendation of a suboccipital approach with the patient sitting, to demonstrate the upper level of a block. Surely a supine lateral C1/C2 approach is less demanding for the paraplegic and tetraplegic patient?

There are minor typographical errors and the flow of text is marred by a too literal translation. The illustrations are outstanding, the index adequate.

There is no doubt that the authors have covered the field of spinal tumours and the book will appeal to a wide audience. However, there is little that is new and is not available in more specialised texts. It is, therefore, difficult to recommend the book strongly on its own, but it will be a useful addition to the series.

C. E. L. Freer

Medical Lasers (science and clinical practice). By J. A. S. Carruth and A. L. McKenzie, pp. xi+261+index, 1986 (Adam Hilger, Bristol), £19.50.
ISBN 0-85274-560-5

The purpose of light is to illuminate and of surgery often to let in the light. It is fitting that this slim volume by a laser physicist and a practising clinical consultant should succeed brilliantly in both.

The first third deals with the physics both of lasers and the production of surgical lesions. This section is aimed at medical physicists and should, according to the dust jacket, be of interest to laser researchers and "the enthusiastic clinician". Certainly for physicists it provides a thorough and concise grounding where, to give one example, I learned the physical significance of the terms "cutting" and "coagulation". There could not, in the space, be sufficient detail on specific lasers for development purposes or for servicing. The clinician will find that enthusiasm does not compensate for a lack of knowledge of Boltzmann statistics.

Most of the rest of the book is a succinct and often critical review of mainly surgical applications. This is clinicians' territory, but is also perhaps the most valuable part for the physicist, because enough background is given to make it readable and unexplained medical terms do not present too much difficulty. Chapters cover ophthalmology, endoscopy, gynaecology, dermatology, otolaryngology, photoradiation therapy, neurosurgery and other surgery including cardiovascular, urological and general surgery. A single clinician cannot be expert in all these fields, with the result that the text does degenerate here and there into a catalogue of references. This is a small penalty to pay for the overall concise, crisp style which probably could not have been achieved if other authors had been co-opted.

The final important chapter on safety covers the topic in a sensible and pragmatic way and all chapters provide extensive references for further reading.

In short, this book is a must for the medical physicist who becomes involved with surgical lasers. It should also be valuable to the clinician who wants a concise overview.

D. H. Follett

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A note on Roentgen's X-ray absorption measurements in 1895

By F. W. Spiers, C.B.E., D.Sc., F. Inst. P.
Formerly of the Medical Physics Department, University of Leeds

(*Received March 1986*)

Among the many observations made by Roentgen in his first paper, the most important and revolutionary for medicine were those on the transmission of X rays through normally opaque materials, notably through tissues of the body. In a single sentence he founded the science of radiology: "If one holds the hand between the discharge apparatus and the screen, one sees the dark shadows of the bones within the much fainter shadow picture of the hand itself" (Roentgen, 1895).

Further absorption experiments were made by Roentgen as well as, in particular, measurements on transmission through metal sheets. In Section 5 of his first paper, Roentgen wrote: "Platinum, lead, zinc and aluminium were rolled out in sheets of such thickness that all appeared nearly equally transparent", the detector being his barium platinocyanide fluorescent screen. He measured the thickness of the sheets and gave the values as in the left-hand part of Table I, which reproduces the table from Roentgen's paper. Besides the thicknesses in mm, he also gave the relative thicknesses and the densities of the metals and commented: "These values show that by no means is the transparency of different metals equal if the product of thickness and density is the same". Elsewhere in his first paper, Roentgen remarked upon the effect of both density and thickness on the transmission of X rays, but nowhere does he mention atomic weight, although it would appear that he had the atomic scale in mind in choosing the four metals for his experiment. Also, it is curious that platinum is placed above lead in the table although it is lower than lead in atomic weight (the concept of atomic number was not formulated at that time).

To investigate the implications of Roentgen's table a little further, I have added in Table I a column giving the product of density and thickness, ρt, and a column giving the reciprocal, $(\rho t)^{-1}$. The values in the last column are roughly proportional to the effective mass absorption coefficients on the simple assumption that $\rho t \cdot (\mu/\rho) = A$ (constant). This, of course, omits consideration of scatter, especially in the case of aluminium, and of the energy dependence of the barium platinocyanide detector, but still, for values of A between 0.5 and 2 (transmissions between 60% and 14%), the coefficients are consistent with modern absorption coefficients for X-ray energies in the range 25–45 keV. The relative absorption coefficient for platinum, however, is 45% greater than that for lead and this, at first sight, appears to be anomalous. The reason probably lies in the occurrence of critical absorption edges in the photoelectric absorption spectra of lead and platinum, as shown in Fig. 1. In the "L" region between 10 keV and 16 keV, the average absorption coefficient for platinum is indeed about 45% greater than that for lead, but very little radiation of this energy would penetrate the wall of the X-ray tube compared with that necessary to obtain a radiograph of the hand. By itself, the L-effect would not be likely to alter greatly the ratio of the average lead and platinum absorption coefficients. On the other hand, in the energy region between the K edges of platinum and lead, at 78.4 keV and 88.0 keV, the platinum photoelectric absorption coefficient is 4.3 times that for lead. If scatter is included, the total absorption coefficient for platinum is 3.8 times the lead value, but the extent to which scatter affected Roentgen's experiment is not known. If 15% of the X-ray energy spectrum lay in the region between platinum and lead K edges, the average photoelectric coefficient for platinum would be 40% greater than that for lead. Whether such conditions held in Roentgen's experiment can only be conjectured; for example, a plausible, lightly filtered, 100 kVp beam could have about 10% of its spectrum in the critical-energy band, but we do not know if Roentgen's "fairly large Ruhmkorff induction coil" could generate potentials of 100 kVp or more, though induction coils of this capability were available at that time. Nevertheless, it seems possible that some part of the X-ray spectrum used by Roentgen lay above the platinum K

TABLE I

ROENTGEN'S MEASUREMENTS OF X-RAY TRANSMISSION IN METALS

Roentgen's original table			Thickness × density (g/cm^{-2})	Reciprocal $cm^2\ g^{-1}$
Thickness	Relative thickness	Density		
Pt 0.018 mm	1	21.5	0.0387	25.8
Pb 0.05 mm	3	11.3	0.0565	17.7
Zn 0.10 mm	6	7.1	0.071	14.1
Al 3.5 mm	200	2.6	0.91	1.10

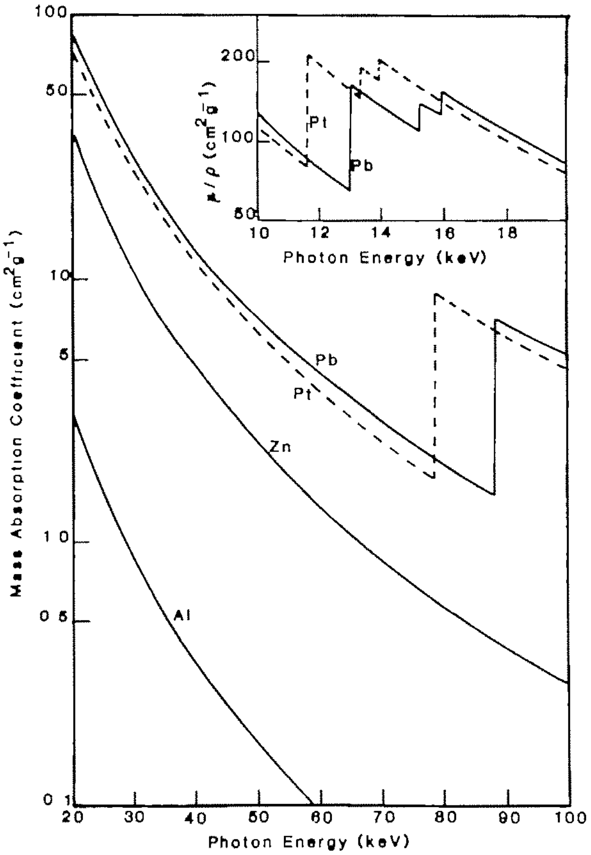

FIG. 1

Mass absorption coefficients for Al, Zn, Pt and Pb Values for Al and Pb from Hubbell (1969); for Zn by extrapolation from Fe and Cu and for Pt by interpolation from data on Pt and Pb by White (1952) and Pb by Hubbell (1969).

absorption edge and this is the most likely explanation of his finding the platinum absorption to be greater than that of lead

Roentgen was a very careful experimenter and unlikely to be mistaken in this observation; nor was he likely to have used very impure materials. Lead might be suspected most of impurity, being at times alloyed with such metals as tin, antimony or bismuth, but these would be unlikely to lower the absorption coefficient sufficiently below that of platinum; bismuth is close to lead in the atomic scale and tin and antimony have absorption edges just above 30 keV, and actually exceed lead in absorption until energies of 88 keV are reached. Below 30 keV tin and antimony absorb much less than lead, but large contaminations, of some 30–40%, are needed to reduce the average mass absorption coefficient of lead to a value as low as 70% of that of platinum.

In the light of these considerations it is understandable that, in terms of X-ray transmission, Roentgen did not find his metals go in rank order with the known atomic scale. It could well be because of this "anomaly" that Roentgen, the cautious scientist, held back from any comment on a possible relationship between X-ray absorption and atomic weight. It is also an intriguing thought that Roentgen's first careful observations of X-ray transmission foreshadowed those later profound discoveries of the X-ray photoelectric effect and Moseley's law.

REFERENCES

HUBBELL, J. R., 1969. *Photon Cross Sections, Attenuation Coefficients, and Energy Absorption Coefficients from 10 keV to 100 GeV.* Report NSRDS–NBS 29 (National Bureau of Standards, Washington, DC).

ROENTGEN, W. C., 1895. On a new kind of rays *Sitzungsberichte der Physikalisch-medizinischen Gesellschaft zu Würzburg.*

WHITE, G R., 1952. *X-ray Attenuation Coefficients from 10 KeV to 100 MeV* NBS Report 1003 (National Bureau of Standards, Washington, DC)

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A graphical method to simplify the application of the linear-quadratic dose–effect equation to fractionated radiotherapy

By R. G. Dale, Ph.D., C.Phys., F.Inst.P.

Department of Medical Physics, Charing Cross Hospital, London W6 8RF

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ABSTRACT

The linear-quadratic (LQ) dose–effect equation has been shown to be capable of providing a number of new insights into clinical radiotherapy. However, even in the most straightforward application of the formalism, *i.e.* to fractionated radiotherapy, the level of mathematics required to solve the associated equations could be a significant barrier to the wider application of the LQ method. In this paper it is shown that a wide range of problems arising in fractionated radiotherapy are capable of being analysed with the aid of one basic graph It is further demonstrated that the extrapolated response dose, which forms the conceptual fulcrum of the LQ method, is an additive quantity, and that the analysis of treatments involving several component parts can be simplified by using this property. The main features of these simplifications are demonstrated using some representative worked examples

A number of recent papers have drawn attention to the potential value of the linear-quadratic (LQ) model as an aid in solving clinical radiotherapy problems involving changes in treatment regimes (*e g.* Barendsen, 1982; Fowler, 1984a; Dale, 1985, 1986a, b). In principle, all treatments can be assessed in terms of total dose (TD), extrapolated response dose (ERD) and relative efficiency per unit dose (RE), the relationship between these three parameters being:

$$\mathrm{ERD} = \mathrm{TD} \times \mathrm{RE} \tag{1}$$

The concepts of ERD and RE may be defined for any type of regime, and their applications have been discussed in previous papers (Barendsen, 1982, Dale, 1985; O'Donoghue, 1986) This communication confines itself to the case of fractionated treatments where the fractions are spaced sufficiently apart to allow full recovery of sublethal damage.

For a conventional fractionation regime:

$$\mathrm{RE} = 1 + D_N/(\alpha/\beta) \tag{2}$$

where the selected α/β ratio is that characteristic of the radiation effect under consideration, and where D_N is the dose/fraction required in N fractions. D_N is related to TD by:

$$\mathrm{TD} = N \times D_N \tag{3}$$

It should be noted that there is no unique value of ERD for any given regime; there will be a number of ERD values, each one related to the various observed radiation responses arising as a result of the particular treatment details, for example, fractionation, irradiation volume and so on. In employing the LQ equations, the basic requirement is to determine the ERD for a specified effect due to a given regime, and subsequently to find other combinations of dose/fraction and total dose which will produce a similar effect; that is, at some stage we need to find the value of D_N which satisfies the equation:

$$N D_N[1 + D_N/(\alpha/\beta)] = \mathrm{ERD} \tag{4}$$

Equation (4), which is obtained by combining Equations (1)–(3), is quadratic in form and, discarding the negative root, leads to a value of D_N given by:

$$D_N = \frac{\sqrt{(\alpha/\beta)^2 + 4(\alpha/\beta)\mathrm{ERD}/N} - (\alpha/\beta)}{2} \tag{5}$$

In everyday applications, regular use of Equation (5) may prove tedious, but problem solving can be made much simpler by adopting a graphical technique. If, for selected values of α/β, D_N is plotted against ERD/N, curves of the type shown in Figs 1A and 1B are obtained. Although all of the curves may be plotted on one graph, it will be found easier and more accurate to use an expanded scale for small values of ERD/N, as is used in Fig. 1A. Taken together, these curves may be used for solving the majority of clinically based problems involving changes in fractionation.

Some worked examples will indicate more clearly how graphical solutions may be found The crucial importance of selecting appropriate α/β values has been discussed elsewhere and will be returned to later in this communication. The hypothetical problems posed here are chosen to illustrate how the proposed method may be applied in practice: the α/β values used should be seen as being broadly representative of the particular effects under discussion, rather than definitive values.

Example 1

An existing treatment regime delivers 60 Gy in 30 fractions. Assuming that late tissue effects are considered to be the limiting factor, and that such effects are characterised by an α/β ratio of 2.5 Gy, what dose/fraction should be employed if 20 fractions are used instead? For the standard regime, $D_N = 60/30 = 2$ Gy/fraction. In Fig. 1A it is seen that, for $\alpha/\beta = 2.5$ Gy, a D_N of 2 Gy/fraction corresponds to

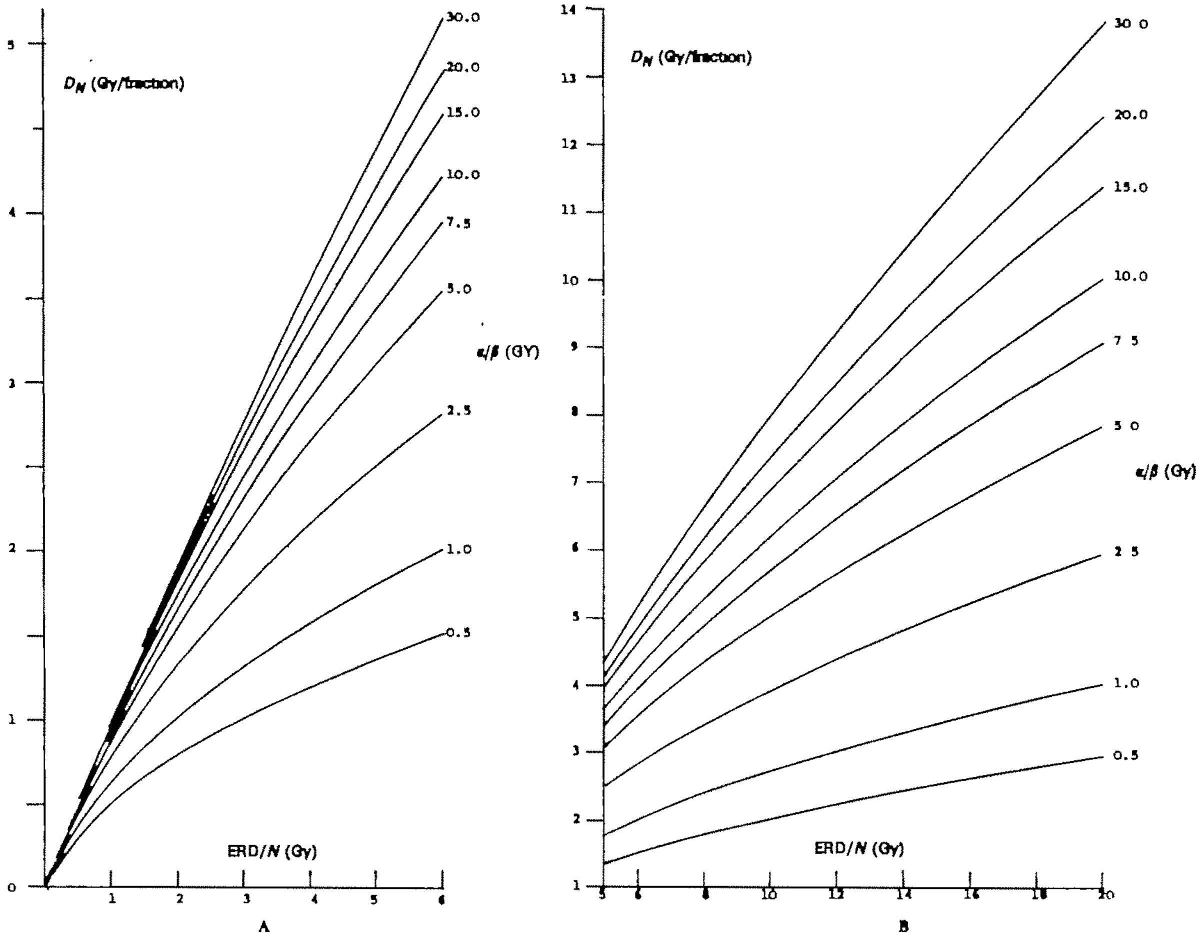

FIG. 1.

(A) Values of D_N versus ERD/N. (ERD/N in the range 0–6 Gy.) (B) Values of D_N versus ERD/N. (ERD/N in the range 5–20 Gy.)

an ERD/N value of 3.6 Gy. Since N is specified to be 30 fractions,

$$\text{ERD} = 30 \times 3.6 = 108 \text{ Gy}$$

To give the same ERD in 20 fractions, the new value of ERD/N to use is 108/20 = 5.4 Gy. Referring in Fig. 1A to the curve for $\alpha/\beta = 2.5$ Gy, we find that the corresponding dose/fraction is 2.64 Gy. Thus, the regime for equivalent *late effects* on the specified tissues is 20 × 2.64 = 52.8 Gy in 20 fractions.

If now we wish to assess the effect of this change in fractionation on, say, the tumour, we can use the graphs with an appropriate tumour α/β value. Let us assume that $\alpha/\beta = 12$ Gy is representative in this case. The ERD for the tumour must be determined first, as it will not be the same as for the late tissue effects.

From Fig. 1A, for the standard regime ($D_N = 2$ Gy),

$$\text{ERD}/N = 2.33 \text{ Gy}$$

i.e.

$$\text{ERD} = 2.33 \times 30 = 69.9 \text{ Gy}$$

To give the same ERD to the tumour in 20 fractions requires that ERD/N = 69.9/20 = 3.5 Gy. Referring again to Fig. 1A for $\alpha/\beta = 12$ Gy, we find that the corresponding dose/fraction is 2.83 Gy.

Therefore, the regime for equivalent *tumour* effects is 20 × 2.83 Gy = 56.6 Gy in 20 fractions. The dose/fraction required is greater than that for equivalent late tissue effects (2.62 Gy/fraction).

This example illustrates how, when the number of fractions is reduced, effects on tissues with relatively high α/β ratios can only be maintained at the expense of extra damage to tissues with lower α/β ratios, *i.e.* late-reacting tissues.

Example 2

An established treatment consists of 25 × 2.25 Gy fractions. Acute-responding tissue reactions (assumed

α/β ratio = 10 Gy) are found acceptable with this regime. It is required to produce the same acute response in a complete course of treatment with a dose/fraction of 1.75 Gy. How many fractions should be given?

From Fig. 1A, with $D_N = 2.25$ and $\alpha/\beta = 10$ Gy, ERD/N = 2.75 Gy. Therefore,

$$\text{ERD} = 2.75 \times 25 = 68.8 \text{ Gy}.$$

With a D_N value of 1.75 Gy/fraction, the corresponding value of ERD/N is 2.05 Gy. Therefore,

$$N = \text{ERD}/2.05 = 68.8/2.05 = 34 \text{ fractions}$$

i.e. the regime for equivalent *early* effects on the specified tissues is 34 fractions × 1.75 = 59.5 Gy.

To assess the effects of this change in fractionation on late-reacting tissues, we can repeat the procedure with an α/β ratio of 2.5 Gy.

For the established treatment, $D_N = 2.25$ Gy. Therefore,

$$\text{ERD}/N = 4.28 \text{ Gy}$$

i.e.

$$\text{ERD} = 4.28 \times 25 = 107 \text{ Gy}$$

At a dose/fraction of 1.75 Gy, the value of ERD/N which would be required for similar late effects is 2.95 Gy, *i.e.*

$$\text{number of fractions} = 107/2.95 = 36$$

Therefore, in this case, the regime for equivalent *late effects* is 36 fractions × 1.75 Gy = 63 Gy, *i.e.* the number of fractions required for equivalent late effects is greater than that required (34) for equivalent early effects.

This example indicates how, when dose/fraction is reduced, if radiation effects on tissues with relatively high α/β are maintained then effects on tissues with lower α/β are reduced.

ADDITIVITY OF ERD AND ITS USE IN MIXED MODALITY TREATMENTS

A problem arises when a treatment is unable to run its prescribed course on account of various extraneous factors, and either dose/fraction or number of fractions has to be changed. A useful property of the LQ formalism which may be used in such cases is the additivity of the components which make up the total ERD in a regime. If a treatment needs to be changed for any reason, the partial ERD already delivered may be calculated, and the remaining ERD "to give" used to determine the remainder of the treatment. Since ERD values can be defined for any constituent part of a complete treatment regime, this additive property can be used in more complex problems, such as combination of external beam and intracavitary therapy. Barendsen (1982) assumed (without formal proof) the additivity of fractions of ERD in his work and applied the property to some treatment examples. By using the basic LQ definitions of radiation damage it is possible to establish a proof of ERD additivity which is true for any type or combination of treatment. The sequence of logical steps leading to the proof is dealt with separately in the Appendix.

Some more examples will aid in understanding the application of this concept. (In these examples the method will be demonstrated for just one α/β ratio in each case. The full assessment of the efficacy of the treatments involves examining other α/β values, as previously indicated.)

Example 3

A patient is prescribed a standard regime of 60 Gy/30 fractions. After 10 fractions it is decided to give the remaining treatment in 12 fractions. What dose/fraction must be employed, assuming that late tissue effects ($\alpha/\beta = 2.5$ Gy) are considered to be the limiting factor?

The ERD for the standard regime has already been calculated (Example 1) and found to be 108 Gy. After 10 fractions, 10/30 = 1/3 of the required ERD has been delivered, therefore, the partial ERD yet to be given is $2/3 \times 108 = 72$ Gy. This is to be delivered in 12 fractions, *i.e.* ERD/N = 72/12 = 6 Gy. Using Fig. 1B, we find that this value of ERD/N is obtained, for effects characterised by an α/β of 2.5 Gy, by using a dose/fraction of 2.8 Gy.

Therefore, the remaining regime is 12 × 2.8 = 33.6 Gy in 12 fractions.

Example 4

A particular treatment for carcinoma cervix consists of four high dose-rate intracavitary treatments interspersed with 12 external beam fractions. The average doses to the rectum from the two modalities are 4 × 6 Gy and 12 × 1.7 Gy, respectively. If two of the intracavitary regimes have to be omitted, what are the possible adjustments that can be made to the external regime, assuming in this case that an equivalent acute epithelial response is required?

Assume that the characteristic α/β value for such effects is 10 Gy, and let the suffixes "cav" and "ext" refer to the intracavitary and external beam treatment, respectively. For the prescribed intracavitary regime, $D_N = 6$ Gy, therefore,

$$\text{ERD}_{\text{cav}}/N = 9.6 \text{ Gy (Fig. 1B)}$$

Since $N = 4$,

$$\text{ERD}_{\text{cav}} = 4 \times 9.6 = 38.4 \text{ Gy}$$

For the external beam regime, $D_N = 1.7$ Gy, therefore $\text{ERD}_{\text{ext}}/N = 2.0$ Gy. Since $N = 12$ in this case, $\text{ERD}_{\text{ext}} = 12 \times 2 = 24$ Gy (Fig. 1B). Therefore, the prescribed regime would deliver a total ERD of:

$$38.4 + 24 = 62.4 \text{ Gy}.$$

If now only two of the intracavitary treatments are given, ERD_{cav} falls to half of the intended value (*i.e.* to

19.2 Gy); therefore, the new value of ERD_{eff} "to give" is:

$$62.4-19.2 = 43.2 \text{ Gy}$$

Appropriate regimes are found by dividing 43 2 by the number of fractions to be given, and finding the new value of D_N via the graph. Examples are:

$$12 \text{ fractions} \times 2.82 \text{ Gy} = 33.8 \text{ Gy}$$
$$18 \text{ fractions} \times 2 \text{ Gy} = 36 \text{ Gy}$$
$$24 \text{ fractions} \times 1.55 \text{ Gy} = 37.2 \text{ Gy}$$
$$30 \text{ fractions} \times 1.27 \text{ Gy} = 38.1 \text{ Gy}$$

As is demonstrated in this case, the graphical method enables a number of alternatives to be established very quickly without recourse to equation solving.

Cautions to be Observed in Applying the Method

In common with other models which are applicable to clinical problem solving, the LQ model is only capable of providing realistic guidelines if its limitations and potential pitfalls are clearly identified. A wider discussion on these aspects has appeared elsewhere (*e.g.* Dale 1985, 1986b), but in relation to the use of the particular system described here for solving fractionation problems, the following points should be remembered.

(a) The unit of dose/fraction, α/β and ERD used in the graphs is the gray (Gy). It is necessary that there is complete conformity of all dose units in using the method, therefore all fractionation details must be expressed in grays before reading the graphs.

(b) Specific values of α/β are not yet available for all tissue effects. General predictions are to hand, however (*e.g.* Fowler, 1984a; Williams et al, 1985), and indicate that:

(1) acute epithelial reactions tend to be characterised by α/β values in the range 8–13 Gy, with an average of around 10 Gy;
(2) late tissue reactions tend to be characterised by α/β values in the range 2–6 Gy, but the spread of values may extend outside this range;
(3) tumour responses tend to be characterised by α/β values in the range 10–25 Gy.

The particular feature of the LQ model is that it enables the effect of altered fractionation to be examined for each of the radiation responses which are usually considered to be of greatest concern, *i.e.* those listed above. However, precise evaluations require precise knowledge of the parameters involved, and these may not be available In such cases, the model is still capable of making broad predictions, for example, of changes in therapeutic ratio, provided prudently selected α/β ratios are used.

In general, in order to obtain a balanced view of the effects of changed fractionation, it is necessary to perform the LQ analysis for at least two values of α/β, these being those which are deemed to be most representative for the particular case under consideration. It will be noted that both tumour and early-reacting normal effects are *generally* represented by a relatively high ratio, while late-reacting effects are *generally* best represented by a relatively low α/β. Two representative values (say 10 Gy and 2.5 Gy, respectively, as used in the examples above) would, therefore, enable an assessment to be made of *likely* changes in therapeutic ratio.

(c) The basic LQ model does not include any allowance for the possible effects of altered cell proliferation resulting from changes in fractionation schedules. In cases where the changes in overall time between regimes is not too great, it is probably in order to assume that such effects are of small significance. Where considerable extensions (or contractions) of treatment time are involved this may not be the case, and some consideration must be given to the likely influence of increased (or reduced) proliferation (*e.g.* Thames et al, 1983; Fowler, 1984b; Thames, 1984; Dale, 1986b).

Discussion

A simple graphical method for applying the LQ formalism to specific problems arising in fractionated radiotherapy has been evolved. The technique is easily mastered and does away with the need to solve quadratic equations routinely. In simplifying the application of the system it is to be hoped that the broader potential of the LQ method, particularly in such areas as assessment of changes in therapeutic ratio, will be made more accessible to clinicians.

In this paper the emphasis has been on discussing conventional fractionated regimes, since it is only for these that it is possible to use the graphical technique. For other treatment types the RE equations are more complex, and similar simplifications in applying the LQ method are not possible in these cases. However, because ERD can be defined for any regime, fractionated or otherwise, and because ERD is an additive quantity, it is possible to analyse mixed-modality treatments (such as protracted intracavitary treatments supplemented with high dose-rate external beam therapy) in greater detail than previously, simply by examining the component parts of the ERD.

Whether or not the LQ formalism is ultimately capable of being as widely used as the CRE/TDF-type models (Kirk et al, 1971; Orton & Ellis, 1973) in practical usage remains to be seen, but there can be no doubt that the newer approach enables a more quantitative view to be taken of the consequences of treatment changes on different radiation effects. This is because the LQ method fully incorporates broadly recognised and quantified differences in radiation response between critical tissues, in the form of the α/β ratio.

The extended model discussed in previous publications, which relates to various forms of protracted treatments (Thames et al, 1984; Dale, 1985), or to treatments involving multiple fractions per day

(Thames, 1985; Dale, 1986b), incorporates only one other parameter, *i.e.* μ, the repair half-life of sublethal injury. The complete LQ formulation is, therefore, self-consistent in analytical terms and does not require, as do some of the earlier models, the introduction of arbitrary constants or normalising factors in order to be of general applicability. This could well be the crucial strength of the LQ model, because any tests applied to it will essentially check the validity of the assumed underlying dose–response model, as there are no other factors introduced simply for the purpose of providing better agreement with clinical data.

REFERENCES

BARENDSEN, G. W., 1982. Dose fractionation, dose rate and iso-effect relationships for normal tissue response. *International Journal of Radiation Oncology, Biology, Physics, 8*, 1981–1997.

CHADWICK, K. H. & LEENHOUTS, H. P., 1973. A molecular theory of cell survival. *Physics in Medicine and Biology, 18*, 78–87.

DALE, R. G., 1985. The application of the linear-quadratic dose–effect equation to fractionated and protracted radiotherapy. *British Journal of Radiology, 58*, 515–528.

DALE, R. G., 1986a. Agreement of quadratic and CRE models in predicting the late effects of continuous low dose-rate radiotherapy (reply). *British Journal of Radiology, 59*, 194.

DALE, R. G., 1986b. The application of the linear-quadratic model to fractionated radiotherapy when there is incomplete normal tissue recovery between fractions, and possible implications for treatments involving multiple fractions per day. *British Journal of Radiology, 59*, 919–927.

FOWLER, J. F., 1984a. Review: total doses in fractionated radiotherapy. *International Journal of Radiation Biology, 46*, 103–120.

FOWLER, J. F., 1984b. What next in fractionated radiotherapy? *British Journal of Cancer, 49*, Suppl. 6, 285–300.

KIRK, J., GRAY, W. M. & WATSON, E. R., 1971. Cumulative radiation effect, 1: fractionated treatment regimes. *Clinical Radiology, 22*, 145–155.

O'DONOGHUE, J. A., 1986. Agreement of quadratic and CRE models in predicting the late effects of continuous low dose-rate radiotherapy. *British Journal of Radiology, 59*, 193–194.

ORTON, C. G. & ELLIS, F., 1973. A simplification of the NSD concept in practical radiotherapy. *British Journal of Radiology, 46*, 529–537.

THAMES, H. D., 1984. Effect-independent measures of tissue responses to fractionated irradiation. *International Journal of Radiation Biology, 45*, 1–10.

THAMES, H. D., 1985. An "incomplete-repair" model for survival after fractionated and continuous irradiations. *International Journal of Radiation Biology, 47*, 319–339.

THAMES, H. D., PETERS, L. J., WITHERS, H. R. & FLETCHER, G. H., 1983. Accelerated fractionation vs hyperfractionation: rationales for several treatments per day. *International Journal of Radiation Oncology, Biology, Physics, 9*, 127–138.

THAMES, H. D., WITHERS, H. R. & PETERS, L. J., 1984. Tissue repair capacity and repair kinetics deduced from multifractionated or continuous irradiation regimes with incomplete repair. *British Journal of Cancer, 49*, 263–269.

WILLIAMS, M. V., DENEKAMP, J. & FOWLER, J. F., 1985. A review of α/β ratios for experimental tumours. *International Journal of Radiation Oncology, Biology, Physics, 11*, 87–96.

APPENDIX

Suppose a standard treatment regime has, for a given level of effect on a specified tissue, an associated extrapolated response dose of ERD_s. Suppose now that N separate regimes are to be given with a view to producing the same combined effect on this same tissue.

Since the effects are to be the same, the lethal (*i.e.* irreparable) damage produced in the standard treatment must be equalled by the sum of the individual irreparable damage components in the N individual regimes.

Let A_s and B_s be, respectively, the Type A and Type B damage produced in the standard regime. Definitions of these two principal types of lethal damage are given by Dale (1985). The definitions themselves are based on the assumption of Chadwick and Leenhouts (1973) that lethal damage is due either to simultaneous "hits" on each of two critical targets (the α component), or due to a lethal combination of the damage inflicted in two separate "hits" (the β component). These are irreparable components, therefore,

$$\text{total damage} = A_s + B_s$$

For the N individual regimes (designated by suffixes 1 to N) to produce the same damage:

$$A_s + B_s = A_1 + B_1 + A_2 + B_2 + \ldots + A_N + B_N \qquad \text{(i)}$$

For the standard regime, where a total dose TD_s is given,

$$\text{ERD}_s = \text{TD}_s \times \text{RE}_s \qquad \text{(ii)}$$

and

$$\text{RE}_s = 1 + (B_s/A_s) \qquad \text{(iii)}$$

Equation (iii) follows from the basic equation for finding RE from Type A and Type B damage (Dale, 1985).

For any component regime, i, the relationships are:

$$\text{ERD}_i = \text{TD}_i \times \text{RE}_i \qquad \text{(iv)}$$

and

$$\text{RE}_i = 1 + (B_i/A_i) \qquad \text{(v)}$$

Therefore, combining the above equations, we have:

$$\text{ERD}_s = \frac{\text{TD}_s}{A_s}\left[\frac{(\text{ERD}_1 \times A_1)}{\text{TD}_1} + \ldots + \frac{(\text{ERD}_N \times A_N)}{\text{TD}_N}\right]$$

i.e.

$$\frac{(A_s \times \text{ERD}_s)}{\text{TD}_s} = \frac{(A_1 \times \text{ERD}_1)}{\text{TD}_1} + \ldots + \frac{(A_N \times \text{ERD}_N)}{\text{TD}_N}.$$

But, as Type A damage is always directly proportional to the total dose delivered, irrespective of the manner in which the dose is given, then:

$A_s = \alpha\text{TD}_s$; $A_1 = \alpha\text{TD}_1$; etc.

Therefore:

i.e. $$\alpha\text{ERD}_s = \alpha\text{ERD}_1 + \alpha\text{ERD}_2 + \ldots + \alpha\text{ERD}_N$$

$$\text{ERD}_s = \text{ERD}_1 + \text{ERD}_2 + \ldots + \text{ERD}_N \qquad \text{(vi)}$$

Equation (vi) shows the additive property of ERD, and is true for all types of treatment, not merely fractionated radiotherapy.

Book reviews

Atlas of Two-Dimensional Echocardiography in Congenital Cardiac Defects. By G. J van Mill, A J. Moulaert and E Harinck, pp 143, 1986 (Martinus Nijhoff, The Netherlands), £26.50.
ISBN 0–89838–783–3

Two-dimensional, or more correctly cross-sectional, echocardiography has advanced the diagnosis of congenital heart disease dramatically over the last few years. I had hoped, therefore, that van Mill and his colleagues in their new textbook would have provided up-to-date knowledge in this field Unfortunately, I was rather disappointed.

The book is a collection of cases collected over 2 years and is not meant to be comprehensive It is divided into 14 chapters, with a good explanatory introduction followed by a concise guide to the anatomy of the normal heart The remaining chapters on abnormal hearts, however, lack any subject depth and are variable in quality There is a considerable amount of contrast echocardiography, which, while still valuable, has only a limited role to play since the introduction of Doppler ultrasound The impact of Doppler studies is hardly mentioned An example of where this is most inappropriate occurs in the chapter on pulmonary stenosis The authors assess the degree of stenosis by the anatomical abnormality of the valve and the degree of right ventricular hypertrophy (both unreliable) without any mention of continuous-wave Doppler There are several other criticisms There is no quantification in the book, there are several omissions, for example Ebstein's anomaly, straddling atrioventricular valves, endomyocardial fibrosis, and there is no index. My copy had Fig. 5.8 on page 78 printed the wrong way round. I would also suspect the book took a long time to produce, as the latest reference included is from 1982, with most dating from 1974 to 1980. Since a large amount of work on the cross-sectional appearances of congenital heart disease has been published since 1982, the edition is somewhat out-dated It fails to provide enough examples or information for the beginner and is not sufficiently advanced for those experienced in the field.

I feel this book, therefore, has limited value.

J. Weir

Pediatric Ultrasonography. Ed. by Gabriel Kalifa, pp. 241, 1986 (Springer-Verlag, Berlin), DM 148.
ISBN 3–540–13085–3 (Berlin)
0–387–13085–3 (New York)

I was pleased to be given the opportunity to review Dr Kalifa's book. I already had a copy in the department and even though it is only 6 months old, it is one of the most thumbed books on the shelves. Gabriel Kalifa and his co-authors present their collective experience of the role of ultrasound in paediatric radiology In his preface, Dr Kalifa claims that the purpose was not to produce an exhaustive text but this book, though small, is indeed a very comprehensive review of the subject, the only omissions being echocardiography, which is deliberate, and hip ultrasound, which is so recent an advance that the book must have been in publication before it became standard practice.

The text is divided into 13 chapters, which deal with an anatomical area, *e.g.*, chest or a system such as the renal tract The first chapter is on antenatal diagnosis There is a brief, sound, practical comment at the end of the chapter on the implications of an antenatal diagnosis of fetal abnormality The authors of the individual chapters present their practical experience and often include an analysis of their case material so that it is easy to assess the relative frequency of conditions. All chapters are well referenced and the index is good. The illustrations are clear and abundant, and the only minor criticism is that many are of B scans and not of modern real-time images Most of the images in the section on head ultrasonography are black on white, while the rest of the images are the more conventional white on black, to which most readers are accustomed This unfamiliar presentation causes some initial difficulty in interpretation These are very minor criticisms and do not detract from a splendid book I read it with enthusiasm and can whole-heartedly recommend it to any department carrying out paediatric ultrasound examinations.

Helen Carty

1986, *The British Journal of Radiology*, 59, 1117–1118

Case reports

Peritonitis mimicking mechanical duodenal obstruction in an infant

By M. A. Sargent, B.Sc., M.R.C.P. (U.K.)

Department of Diagnostic Radiology, Stopford Medical School, Manchester M13 9PT

(*Received February 1986*)

Bilious vomiting is a common symptom of systemic disease in infancy but it is also the cardinal symptom of mechanical duodenal obstruction. Paralytic or adynamic ileus in the adult may reproduce the radiological signs of duodenal obstruction, but such an event in childhood has not been described in the radiological literature. The case of an infant in whom bilious vomiting due to primary peritonitis led to the erroneous radiological diagnosis of mechanical obstruction of the duodenum with volvulus is described.

CASE REPORT

A nine-week-old boy presented with a 6-day history of swelling of the left leg and groin. There was no pyrexia and he was not systemically unwell, but dilated superficial veins were noted over the oedematous groin and lower abdominal wall. The clinical features and associated neutrophil leucocytosis led to a diagnosis of femoral venous thrombosis secondary to infection, although no causative organism was identified. Accordingly, intravenous antibiotic therapy was commenced. He remained quite well until 3 days later, when there was sudden clinical deterioration with bilious vomiting and abdominal distension. A "septic screen" including cerebrospinal fluid and urine culture again showed no new evidence of infection.

Plain abdominal radiography showed only non-specific abnormality with a general paucity of intestinal gas and isolated bowel loops. A barium meal study revealed dilatation of the proximal duodenum with abrupt transition to normal in the third part (Fig. 1). On fluoroscopy, to-and-fro peristaltic movements between the dilated duodenal segment and the stomach were observed. The duodeno-jejunal flexure lay in the appropriate position to the left of the midline.

A pre-operative diagnosis of partial duodenal obstruction with midgut volvulus was reached and the child underwent urgent surgery. Laparotomy, however, revealed no evidence of intrinsic or extrinsic mechanical duodenal obstruction, nor of volvulus. Instead, there was a generalised staphylococcal peritonitis secondary to intraperitoneal rupture of a left-sided pelvic abscess. After peritoneal lavage the abdomen was closed and the patient made an uneventful recovery, continuing the pre-operative antibiotic regimen. Investigation identified no other site of infection.

DISCUSSION

Both of the terms "duodenal obstruction" and "duodenal ileus" have been employed synonymously to describe a syndrome characterised by bilious vomiting and duodenal dilatation (Hearn, 1966). In adult practice, the syndrome has been shown to exhibit similar appearances on contrast radiology with both mechnical and non-mechanical aetiologies. To establish the diagnosis, it is not necessary to demonstrate complete duodenal obstruction, and distal gas or contrast agent may be observed (Anderson et al, 1982). Since the symptoms of duodenal obstruction may be intermittent, and the radiological signs transient, the upper gastrointestinal study is best performed in the symptomatic patient under close fluoroscopic control (Bitner, 1958; Poznanski, 1976). Diagnostic features include duodenal dilatation going on to gastric distension, abrupt change in duodenal calibre, often with a vertical linear zone of transition, and visible to-and-fro ("reverse") peristalsis (Hearn, 1966).

Thus, the radiological signs elicited in our case were clearly consistent with a diagnosis of duodenal obstruction. The usual gamut of causes of duodenal obstruction in childhood is confined to mechanical lesions, of which congenital anomalies form the greater part (Koo-Sang et al, 1982). Intrinsic congenital duodenal abnormalities are more frequent than extrinsic, 90% present in the first day of life, and the great majority are confirmed radiologically on the plain-radiographic demonstration of the duodenal "double bubble" (Salonen, 1978). Extrinsic congenital duodenal obstruction tends to present later, although 75% are still diagnosed in the first 2 months. In these patients,

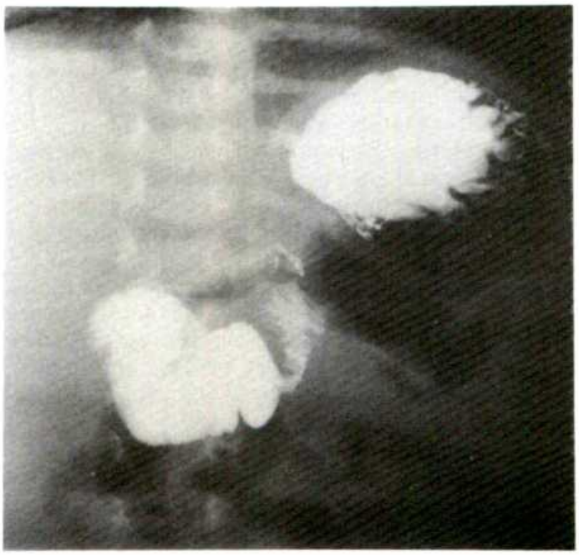

FIG. 1.

Radiograph taken during a barium meal showing proximal duodenal dilatation with a narrow transition zone.

an upper gastrointestinal series is usually required to establish the diagnosis (Salonen, 1978).

Peritoneal bands with or without intestinal rotation anomalies comprise the majority of the causes of extrinsic duodenal obstruction in children (Wayne & Burrington, 1973). The radiological signs of these extrinsic duodenal lesions include partial duodenal obstruction, abnormal position of the duodeno-jejunal flexure and abnormal position of proximal jejunal loops While any one of these signs alone is sufficient to suggest the presence of malrotation, the diagnosis is all too seldom made before surgery (Simpson et al, 1972).

Midgut volvulus is the most feared complication of malrotation, and may be clinically silent. A pathognomic spiral of contrast agent may be seen on contrast study in small-bowel volvulus, but more often only the signs of extrinsic duodenal obstruction can be found. No diagnostic features of volvulus are recognised on plain abdominal radiographic series, but paucity of abdominal gas in the appropriate clinical setting is regarded as highly suspicious (Simpson et al, 1972). In view of the non-specificity of the signs of midgut volvulus, the demonstration of incomplete duodenal obstruction is taken as an indication to proceed to early surgery to exclude potentially fatal and unrecognised volvulus.

Thus, in the present case, there were clinical signs of an acute abdomen, with radiological evidence of duodenal obstruction and also plain-radiographic abnormalities These features led to the diagnosis of midgut volvulus which was not confirmed at surgery. Since no obstructing lesion was identified, ileus was implicated in the pathogenesis of the duodenal obstruction.

Adynamic ileus due to inflammatory conditions such as peptic ulceration and acute pancreatitis is a recognised cause of duodenal obstruction in adults (Cimmino, 1961) Simon and Lerner (1962), however, postulated that the phenomenon could be explained by oedema of the root of the mesentery While generalised intestinal ileus, sometimes mimicking a surgical emergency, is well known to occur in systemic illness in the neonate (Dunn, 1963; Ueda et al, 1968), duodenal obstruction due to paralytic ileus in children is not described in the radiological literature.

Raffensperger et al (1961) reported two cases of erroneous barium-meal diagnosis of gastric outlet obstruction in neonates vomiting because of other systemic disorders. In a third instance, mechanical duodenal obstruction was falsely suggested by an air contrast study in an infant suffering from maternal heroin withdrawal Of these three patients, two went on to have needless surgery. Fortunately, the erroneous diagnosis in our patient did not adversely affect the management. The possibility of a functional ileus mimicking mechanical duodenal obstruction in the child should be considered before arriving at a diagnosis that will commit the patient to surgery.

ACKNOWLEDGMENT

I thank Mr D C. S. Gough and Dr S. C. Gupta of the Royal Manchester Children's Hospital for their permission to report on this patient who was in their care

REFERENCES

ANDERSON, J R, EARNSHAW, P M. & FRASER, G M., 1982. Extrinsic compression of the third part of the duodenum *Clinical Radiology, 33,* 75–81

BITNER, W P., 1958. Arteriomesenteric occlusion of the duodenum. *American Journal of Roentgenology, Radium Therapy and Nuclear Medicine, 79,* 807–814.

CIMMINO, C. V, 1961. Arteriomesenteric occlusion of the duodenum; an entity? *Radiology, 76,* 828–829.

DUNN, P M.. 1963. Intestinal obstruction in the newborn with special reference to transient functional ileus associated with respiratory distress syndrome. *Archives of Disease in Childhood, 38,* 459–460

HEARN, J B, 1966 Duodenal ileus with special reference to superior mesenteric artery compression. *Radiology, 86,* 305–310

KOO-SANG, O. H, LEDESMA-MEDINA, J & BENDER, T. M., 1982 In *Practical Gamuts and Differential Diagnosis in Pediatric Radiology* (Year Book Medical Publishers, Chicago), p. 107.

POZNANSKI, A. K, 1976 In *Practical Approaches to Pediatric Radiology* (Year Book Medical Publishers, Chicago), p 113.

RAFFENSPERGER, J., JOHNSON, F R. & GREENGARD, J., 1961. Non-mechanical conditions simulating obstructive lesions of the intestinal tract in the newborn infant. *Surgery, 49,* 696–700.

SALONEN, I S, 1978. Congenital duodenal obstruction *Acta Paediatrica Scandinavica,* (Suppl. 272), 1–87.

SIMON, M & LERNER, M. A., 1962 Duodenal compression by the mesenteric root in acute pancreatitis and inflammatory conditions of bowel. *Radiology, 79,* 75–80.

SIMPSON, A J., LEONIDAS, J C., KRASNA, I H., BECKER, J. M & SCHNEIDER, K M., 1972. Roentgen diagnosis of midgut malrotation: value of upper gastrointestinal radiographic study. *Journal of Paediatric Surgery, 7,* 243–252.

UEDA, T, OKAMOTO, E. & SEKI, Y., 1968 Non-mechanical intestinal obstruction simulating surgical emergency in the newborn infant. *Journal of Paediatric Surgery, 3,* 676–681.

WAYNE, E. R. & BURRINGTON, J D., 1973. Management of 97 children with duodenal obstruction *Archives of Surgery, 107,* 857–860.

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Case reports

Imaging of a case of sclerosing panniculitis

By J. Stack, M.R.C.P.I., F.F.R. (R.C.S.I.), *S. J. Heffernan, F.R.C.S.I., †P. Dervan, M.D., M.Sc., M.R.C.Path. and ‡J. T. Ennis, M.D., F.R.C.P.I., F.R.C.R.

Institute of Radiological Science, *Department of Surgery, †Department of Pathology, Mater Misercordiae Hospital, Dublin 7, Republic of Ireland

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Sclerosing panniculitis is an idiopathic inflammatory condition occurring most commonly in the adipose tissue of the mesentery. It is characterised by inflammation and fibrosis usually resulting in a tumour-like mass. Both of the components may be the expression of different stages of their reparative process (Reske & Namiki, 1975) and although limited to the mesentery of the small bowel, one case of primary omental involvement has been reported (Durst et al, 1977).

The pathogenesis and epidemiology of sclerosing panniculitis is unknown but previous abdominal surgery and associated intra-abdominal disease are thought to be involved in the development of the non-specific, inflammatory reaction of the fatty tissue, resulting in sclerosis (Durst et al, 1977).

Sclerosing panniculitis may occur in other sites when associated with systemic diseases, such as Weber-Christian disease (Handelsman & Shelley, 1965). However, 60% of cases are confined to the abdomen where it is a rare cause of an abdominal mass; we now report a second case of exclusive omental involvement.

CASE REPORT

A 60-year-old woman complaining of abdominal pain, anorexia and general malaise was admitted to hospital. At examination the patient was mildly pyrexial, with an ill-defined, central, slightly tender abdominal mass. There were no other relevant clinical features. Laboratory tests revealed normal haematological and biochemical findings with a white cell count of 11.5×10^3 and an erythrocyte sedimentation rate of 25 mm/h.

Radiological findings

A plain abdominal radiograph and barium enema were normal. A CT examination demonstrated a large mass measuring approximately 18 cm × 7 cm, lying anteriorly and obliterating the interface between the ascending colon, small bowel and anterior abdominal wall (Fig. 1). The soft-tissue mass was heterogeneous with ill-defined regions containing material of fat density. Following intravenous contrast medium injection, there was minimal edge enhancement. The findings were considered to be consistent with either an inflammatory mass or an extensive mesenteric or omental neoplasm.

An indium-111 tropolone scan was performed using a standardised technique (Thakur et al, 1977) in which scans were obtained at 2, 4 and 24 h after the injection of indium-111

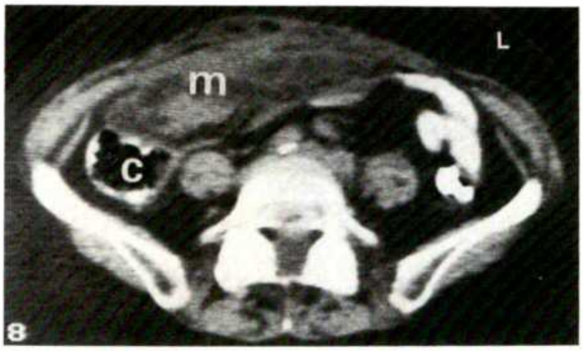

FIG. 1.

A CT section midabdomen demonstrating the mass (M) with loss of interface between ascending colon (C), small bowel and anterior abdominal wall.

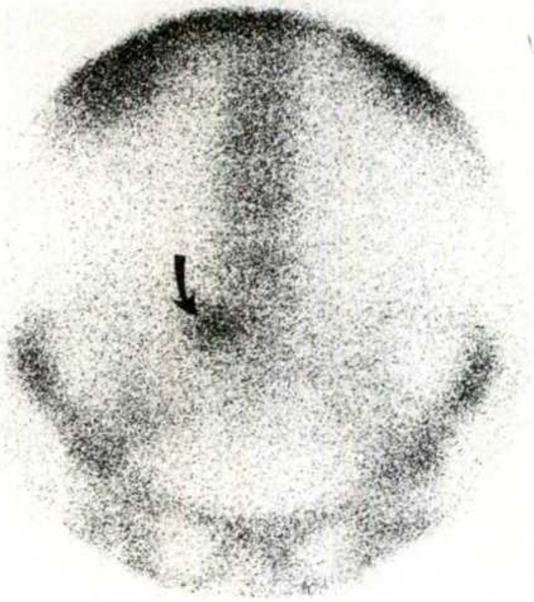

FIG. 2.

Indium-111 tropolone scan at 24 h after injection showing focal uptake (arrow).

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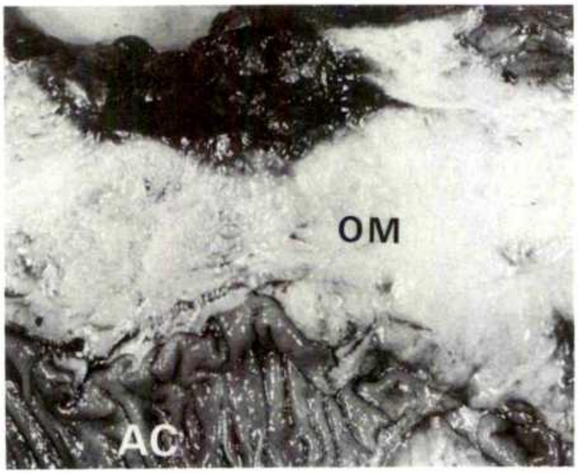

FIG. 3.

Resected omental mass (OM) and ascending colon (AC).

tropolone leucocytes. At 2 h, a localised region of increased uptake was noted in the right mid-abdomen which intensified and became very localised at 24 h (Fig. 2). Needle aspiration at the site of maximum uptake was attempted, but no pus was obtained.

At laparotomy a large, firm, fibro-fatty omental mass peeled off the anterior abdominal wall but was adherent to the mesentery and ascending colon. The mass was mobilised and resected complete with the ascending colon (Fig. 3). The peritoneum was firmly adherent to the involved mesentery and could not be stripped off. The patient made an uneventful recovery and was discharged well.

Pathological examination of the resected specimen revealed an 18 cm × 10 cm × 6 cm firm white mass infiltrating the serosa and muscularis propria of the ascending colon extending into the omentum. The mucosa was entirely normal and there were no diverticula present. Microscopic examination showed that the mass was composed of inflammatory cells and dense, collagenous tissue. There was no evidence of abscess formation and no granuloma was identified (Fig. 4).

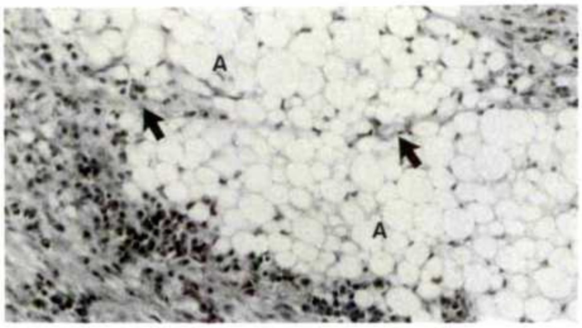

FIG. 4.

Omentum showing a bundle of fibrous tissue with a mixed inflammatory infiltrate dissecting fatty lobules (arrows) (haematoxylin and eosin × 28). A = adipose tissue.

DISCUSSION

The pre-operative diagnosis of primary solid masses of the mesentery or omentum is difficult as clinical and pathological findings are frequently non-specific. The pre-operative diagnosis of sclerosing panniculitis is rarely possible (Reske & Namiki, 1975). Although 15% of patients may present with a leucocytosis, haematological and laboratory investigations are not helpful in the diagnosis (Ogden et al, 1965).

Plain radiographs of the abdomen are of limited value and in only a minority of patients in whom the abdominal mass has displaced the bowel or given rise to partial intestinal obstruction (Ogden et al, 1965). The most useful diagnostic aids before CT scanning were gastrointestinal barium studies but these, too, were non-specific, simply showing either partial obstruction or displacement of bowel loops in approximately one-third of patients (Durst et al, 1977).

Computed tomography accurately shows the site, size and extent of the mass and, as in this case, any involvement of neighbouring structures. It fails, however, to differentiate between neoplastic and inflammatory masses, and several conditions have similar, non-specific CT features, making differentiation of sclerosing panniculitis difficult.

The fibromatosis, if localised, may present as an abdominal mass. The more important of this diverse group of infiltrating fibroblastic proliferative disorders is the musculo-aponeurotic fibromatosis or desmoid tumours which can occur on the anterior abdominal wall (Sacks et al, 1978). However, this tumour contains no fat and is readily distinguishable on CT. Similarly, the mesenteric or omental desmoids associated with Gardner's syndrome also consist of well differentiated fibroblasts of uniform size. Inflammatory infiltration is not a feature (Mackenzie, 1972).

Neoplasms associated with diffuse desmoplastic changes, such as carcinoid tumours, abdominal lymphoma or carcinomatosis, may produce mesenteric or omental masses which may be difficult to differentiate from fatty mesenteric tumours. Angiomyelolipomas and teratomas may be suggested on the basis of their extraperitoneal site and, in the case of teratoma, by the presence of cysts or calcified material within the lesion. Other lipomatous tumours, such as the liposarcoma, are usually large, of non-uniform density, with randomly distributed fatty elements which may resemble sclerosing panniculitis, but, unlike panniculitis, most liposarcomas are sharply defined, being separated from adjacent structures by distinct cleavage planes (Waligore et al, 1981).

In sclerosing panniculitis, the pathological process involves the mesenteric or, as in this case, omental fat. The various descriptive terms used to characterise this process stem from histological differences emphasised by various authors (De Castro et al, 1967). Aach et al (1968) described the presence of lipid-laden macrophages and round-cell infiltrates distributed in broad bands, *i.e.* a dominantly inflammatory process characterised by cellular infiltration. The term "retractile mesenteric sclerosis" is generally reserved for those with a more chronic course, complicated by fibrosis and retraction. Histologically, our case falls into the subacute group of cellular infiltration, which explains the uptake of indium-tropolone labelled white cells.

The CT features of sclerosing panniculitis were confirmed at surgery, but CT failed to differentiate between a neoplastic and inflammatory mass. To avoid unnecessary and extensive surgery it is important to attempt to differentiate inflammatory lesions from other causes of mesenteric masses.

A CT scan will usually provide little more than anatomical localisation, but an indium-111 leucocyte scan will also help to distinguish inflammatory from other mesenteric or omental masses.

REFERENCES

AACH, R. D, KAHN, L. I. & FRISCH, R. S., 1968. Obstruction of the small intestine due to retractile mesenteritis *Gastroenterology, 54*, 594–598

DE CASTRO, J. A, CALEM, W S. & LYCOUROGOS, P., 1967 Liposclerotic mesenteritis. *Archives of Surgery, 94*, 26–29.

DURST, A. L., FREUND, H, ROSENMANN, E. & BIRNBAUM, D., 1977. Mesenteric panniculitis. a review of the literature and presentation of cases *Surgery, 81*, 203–211.

HANDELSMAN, J. C. & SHELLEY, J., 1965. Mesenteric panniculitis *Archives of Surgery, 91*, 846–850.

MACKENZIE, D H., 1972. The fibromatoses: a clinicopathological concept. *British Medical Journal, iv*, 277–281.

OGDEN, W. W., BRADBURN, D, M & RIVES, J. D., 1965. Mesenteric panniculitis a review of 27 cases. *Annals of Surgery, 161*, 864–873

RESKE, M. & NAMIKI, H, 1975 Sclerosing mesenteritis—report of two cases. *American Journal of Clinical Pathology, 64*, 661–667

SACKS, B, JOFFE, N & HARRIS, N., 1978 Isolated mesenteric desmoids (mesenteric fibromatosis) *Clinical Radiology, 29*, 95–100

THAKUR, M., LAVENDER, J. P, ARNOT, R. N., SILVESTER, D. J. & SEGAL, A W, 1977. Indium-111 labelled autologous leucocytes in man. *Journal of Nuclear Medicine, 18*, 1014–1021.

WALIGORE, M. P., STEPHENS, D H., SOULE, E. H & MCLEOD, R A, 1981 Lipomatous tumors of the abdominal cavity: CT appearance and pathologic correlation. *American Journal of Roentgenology, 137*, 539–545.

Candida abscess of the pancreas: diagnosis and treatment by computed tomography-guided percutaneous drainage

By *E. J. Fitzgerald, M.R.C.P., F.R.C.R. and K. Lyons, M.B., B.Ch.

Department of Diagnostic Radiology, University Hospital of Wales, Heath Park, Cardiff CF4 3XW

(Received March 1986)

Candida albicans is found frequently as a commensal organism in the gastrointestinal tract. Despite this, it is rarely found in pancreatic abscesses, there being less than 10 cases in the literature (Richter et al, 1982). We report the case of a patient in whom computed tomography (CT) was used initially to diagnose a pancreatic fluid collection complicating a splenectomy. Computed tomography was then used during diagnostic aspiration followed by definitive treatment of what was shown to be an abscess by placement of a percutaneous drainage catheter under CT guidance.

CASE REPORT

A diagnosis of myelofibrosis was made 15 months before splenectomy in a 65-year-old man. Splenectomy had been decided upon because of the necessity of more frequent blood transfusions and the increasing size of the spleen, with associated pain. At operation, numerous adhesions were found between the spleen, peritoneum and abdominal organs. The tail of the pancreas extended into the hilum of the spleen The resected spleen weighed 2400 g (normal c. 400 g) and microscopic examination showed changes compatible with myelofibrosis. A second laparotomy was required within 24 h because of bleeding vessels in the region of the body of pancreas

Over the next 3 weeks the patient remained unwell, continued to lose weight and required two further operations for bleeding problems. During this time he was treated with broad-spectrum antibiotics, but he remained pyrexial A few days after his fourth operation, a CT scan showed a fluid-filled cavity in his left upper quadrant. Fluid was aspirated under CT guidance using a fine needle and was found to contain over 200 000 units of amylase/l. Microscopic examination showed fungal elements and, because the fluid was infected, percutaneous catheter drainage was performed (Fig 1) Sinography showed no communication with the lumen of the bowel A total of 640 ml of brownish fluid was drained over the following 24 h and culture of the original aspirate confirmed the presence of *Candida albicans*, which was resistant to ketoconazole, so intravenous and intracavity therapy with amphotericin B was started. Symptomatic improvement was evident within 24 h of drainage and his temperature returned to normal within 36 h. Large amounts of fluid were drained over 6 days, gradually decreasing over the

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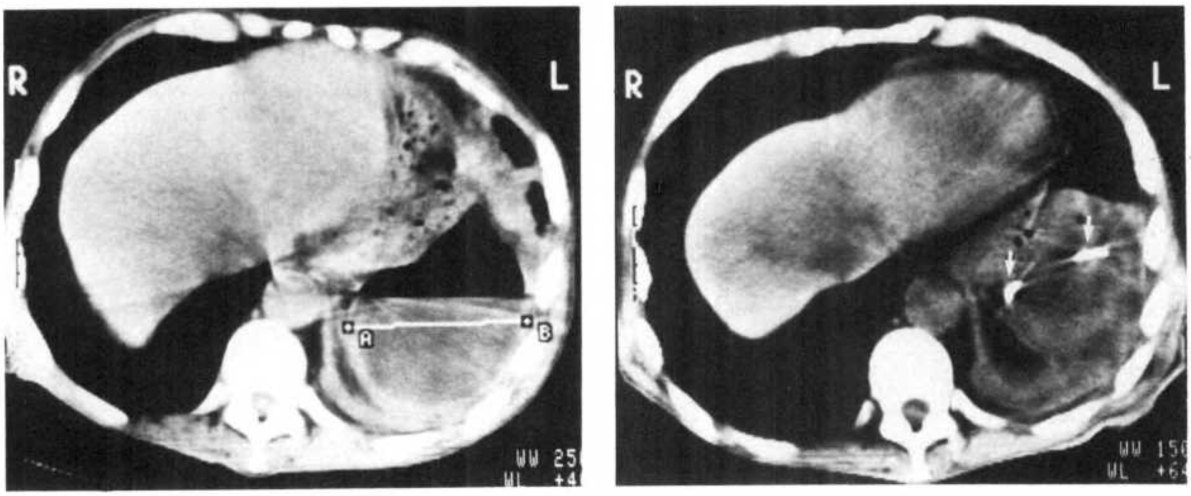
*Author for reprint requests.



A

B

FIG. 1.

(A) Large fluid-containing mass in the splenic bed found to contain amylase and fungi on aspiration. (Note gas following needle drainage.) (B) Repeat scan 2 weeks later, showing the drainage catheter *in situ* (arrows) with great reduction in the size of the cavity.

following 20 days. The drainage tube was removed at 26 days, the patient having gone home on the eighteenth day.

He returned to his normal weight of 74 kg (from 54 kg at the time of drainage) within 3 months.

The patient still requires blood transfusion at approximately 4-monthly intervals, but otherwise remains well 18 months after drainage.

DISCUSSION

Deep *Candida* infections rarely occur in the intact host, but their incidence has increased greatly in immunosuppressed patients, especially those who have been treated with cytotoxic drugs. The incidence of such infection is also increased in patients who are debilitated or following surgery or treatment with broad-spectrum antibiotics (Gregory, 1982). Despite its frequent presence in the bowel, *Candida albicans* is rarely found in pancreatic abscesses (Richter et al, 1982). The organisms involved in infected pancreatic abscesses are generally enteric, although the mechanism by which they reach the pancreas is unclear in most instances (Ranson et al, 1985). *Candida* is known to penetrate the normal gastrointestinal tract (Gregory, 1982) and this may be the route of infection in our patient. Transvenous infections also occur, but there was no evidence of *Candida* contamination in any of our patient's intravenous lines, and multiple blood cultures were sterile. The patient had had major surgery, was debilitated (weight loss 20 kg), had been treated with antibacterial drugs and had intravenous lines; he thus had multiple reasons for *Candida* infection.

Inadvertent pancreatic injury occurs in a significant number of patients undergoing splenectomy, especially if the operation is technically difficult, as is often the case with massive splenomegaly. The close relationship between the tail of the pancreas and the spleen is felt to be the main reason for the high incidence of left upper quadrant fluid collections post-operatively (Balthazar et al, 1985). Computed tomography is the method of choice for demonstration of these collections, especially if they are in the region of the pancreatic tail or in the lesser sac.

Pancreatic abscess is a serious complication of pancreatitis, with a high mortality rate. Only 41% of patients survived in one series, all of whom underwent surgery (Kaushik et al, 1984). Abscess complicates post-operative pancreatitis (40%) more frequently than alcoholic (4%) or biliary pancreatitis (7%) (Hill et al, 1983). A diagnosis of pancreatic abscess can be suggested radiologically when, either on plain radiographs or CT, gas can be seen within the pancreas or pancreatic mass. Gas can also be seen in such collections when fistulous communication occurs with the gastrointestinal tract (Torres et al, 1981). Fluid-containing pancreatic abscess without gas cannot be distinguished from uncomplicated "pseudocyst" or old areas of haemorrhage on CT appearances alone (Hill et al, 1983; Balthazar et al, 1985). Diagnostic percutaneous aspiration should be performed on such collections if an abscess is suspected (as in our case) (Hill et al, 1983). Such percutaneous aspiration can also be used for injection of contrast medium to demonstrate fistulous connection between the mass and the bowel if this is suspected (Torres et al, 1981).

If infection is found after aspiration, the abscess can be treated by percutaneous catheter drainage (Karlson

1986, *The British Journal of Radiology*, *59*, 1123–1125 NOVEMBER 1986

et al, 1982). Guidance by CT is the method of choice in demonstrating a safe access route for drainage of such abscesses, which can be an important temporising measure in moribund patients and may occasionally (as in our case) be curative. It is important to follow the progress of drainage closely, measuring the amount drained and supplemented by sinography, CT or ultrasound at approximately weekly intervals. Lack of improvement or deterioration in the patient's condition is an indication for surgery (Karlson et al, 1982).

We wish to stress the importance of considering the possibility of *Candida* infection in patients who have the predisposing factors described above. If there is clinical suspicion of this or any other type of infection in a pancreatic or peripancreatic fluid collection then percutaneous diagnostic aspiration is necessary. Computed tomography can be used to demonstrate a safe access route for percutaneous catheter drainage and to monitor the progress of such treatment.

REFERENCES

BALTHAZAR, E. J., MEGIBOW, A., ROTHBERG, M. & LEFLEUR, R. S., 1985. CT evaluation of pancreatic injury following splenectomy. *Gastrointestinal Radiology*, *10*, 139–144.

GREGORY, D. W., 1982. Saturday conference: candida infections. *Southern Medical Journal*, *75*, 339–345.

HILL, M. C., DACH, J. L., BARKIN, J., ISIKOFF, M. B. & MORSE, B., 1983. The role of percutaneous aspiration in the diagnosis of pancreatic abscess. *American Journal of Roentgenology*, *141*, 1035–1038.

KARLSON, K. B., MARTIN, E. C., BANKUCHEN, E. I., MATTHEN, R. P., SCHULTZ, R. W. & CASARELLA, W. J., 1982. Percutaneous drainage of pancreatic pseudocysts and abscesses. *Radiology*, *142*, 619–624.

KAUSHIK, S. P., VOHRA, R., VERMA, G. R., KAUSHIK, S. & SABMARWAL, A., 1984. Pancreatic abscess: a review of seventeen cases. *British Journal of Surgery*, *71*, 141–143.

RANSON, J. M. C., BALTHAZAR, E., CACCAVALE, R. & COOPER, M., 1985. Computed tomography and the prediction of pancreatic abscess in acute pancreatitis. *Annals of Surgery*, *201*, 656–663.

RICHTER, J. M., JACOBY, G. A., SCHAPIRO, R. H. & WARSHAW, A. L., 1982. Pancreatic abscess due to candida albicans. *Annals of Internal Medicine*, *97*, 221–222.

TORRES, W. E., CLEMENTS, L., SONES, P. J. & KNOPF, D. R., 1981. Gas in the pancreatic bed without abscess. *American Journal of Roentgenology*, *137*, 1131–1133.

Liver lesions in histiocytosis X: findings on sonography and computed tomography

By M. Päivänsalo and H. Mäkäräinen

Department of Diagnostic Radiology, University Hospital of Oulu, Finland

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Histiocytosis X is a disease of the lymphoreticular system of unknown aetiology, characterised by histiocytic infiltration of one or more tissues (Lichtenstein, 1955). Lipids, mainly cholesterol, are often present in the histiocytic deposits (Anderson & Scotti, 1972). The usual radiological findings of histiocytosis X are skeletal translucencies, pulmonary infiltrations, honeycomb lungs and signs of lymphadenopathy (Sutton, 1980; Vanel et al, 1983). We describe a case with liver lesions, examined by sonography and computed tomography (CT).

CASE REPORT

A reindeer-herder, born in 1961, had been suffering since 1977 from skin rash, diabetes insipidus, panhypopituitarism and respiratory symptoms; latterly there had been persistent icterus and progressive neurological symptoms. An axillary node and a skin lesion were removed in 1981 and a swollen submandibular gland in 1984; all showed histological evidence of histiocytosis X. Skull radiographs showed sharply demarcated translucencies in the region of the mastoid and in the mandible. A suprasellar expansion was monitored by CT and observed to be slowly growing. New, dense, focal cerebral lesions were found in June 1985. Chest radiographs showed temporary pulmonary infiltrations and bullous emphysema with occasional pneumothorax. Skeletal scintigraphy revealed increased uptake in the skull and left sacro-iliac region. Serum transaminases were elevated for about 7 years, and liver biopsies in 1981 and 1983 revealed focal histiocytic lesions. Echo-dense zones were seen around the portal branches in the liver on sonography in February 1984. Seven months later these had widened considerably (Fig. 1). In February 1984, CT showed hypodensity in the same areas, which 7 months later had enlarged and assumed the density of fat (Fig. 2).

The patient was given hormone substitution (levothyroxin, hydrocortisone and desmopressin). The suprasellar tumour was treated by local radiotherapy in 1983 and the new cerebral lesions by whole-skull radiotherapy in June 1985. He received methotrexate-prednisolone chemotherapy for 2 months (March and April 1984) without improvement and this was stopped because of elevated serum transaminases. Chemotherapy was continued with vinblastine but the disease progressed and the patient died in November 1985. Autopsy was not done.

DISCUSSION

The term histiocytosis X is used for diseases of the reticuloendothelial system characterised by infiltration of histiocytes, which may concentrate cholesterol or

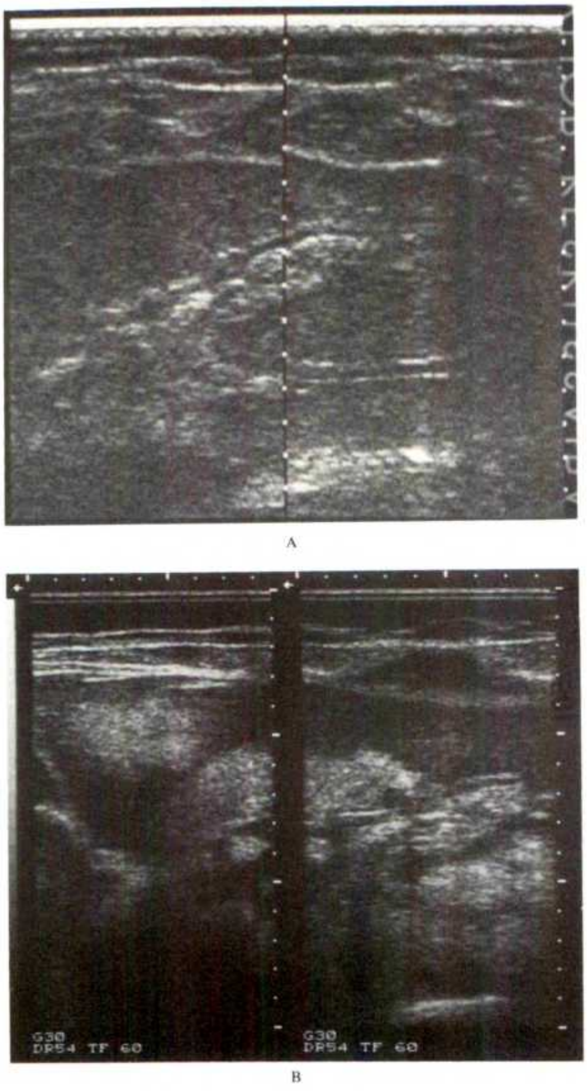

Fig. 1.

Sonogram. Echo-dense zones are seen around the portal branches in the liver in February 1984 (A) and have progressed markedly 7 months later (B).

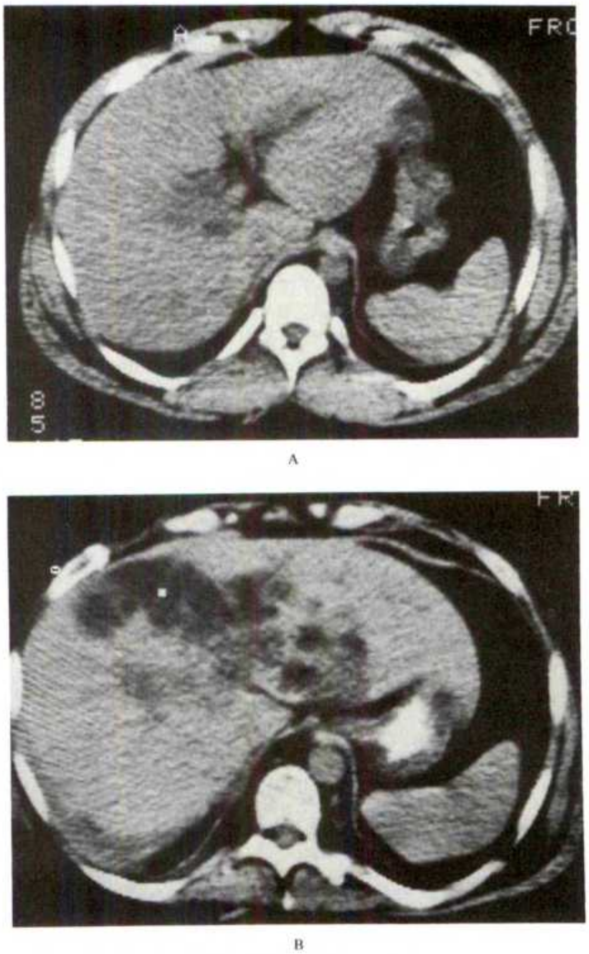

Fig. 2.

Computed tomogram. Hypodense areas are seen around the portal branches in February 1984 (A): 7 months later the areas have increased in size and have the density of fat (B).

similar material. Three somewhat different clinical and morphological variants of histiocytosis X are Letterer-Siwe disease, Hand-Schüller-Christian disease and eosinophilic granuloma (Kellinghaus et al, 1982). Letterer-Siwe disease is a rapidly fatal disease of infancy in which virtually any organ can be affected. Hand-Schüller-Christian disease is a more chronic form which characteristically involves bone, especially the skull, but sometimes also involves the skin, liver, spleen, lymph nodes and lungs. Eosinophilic granuloma, the most benign variant, is usually seen as a bone lesion. In this case the patient had Hand-Schüller-Christian disease.

Relatively few changes have been recorded in the abdominal organs, although the lymphographic appearances of histiocytosis X have been described (Von Renner, 1975; Musaji & Parsons, 1983). Elevated serum transaminase, hepato- and splenomegaly have been recorded as evidence of damage to these organs (Kellinghaus et al, 1982; Vanel et al, 1983; Mišiková et al, 1984). Mourad et al (1983) reported the CT finding of extravisceral, diffuse infiltration of adult histiocytosis X appearing as a large mass surrounding the pancreas, kidneys and adrenals with thickening of the mesentery. In their case, enlargement of the liver, spleen and kidneys was the result of obstruction of the draining vessels. Wood et al (1984) reported a rapidly fatal case of histiocytosis X with negative liver and spleen scans; a few months later autopsy showed massive infiltration of the lungs, liver, spleen, kidney and lymph nodes with histiocytic foci in the myocardium, skin, kidney and bladder. In our case, the liver was not enlarged, but serum transaminases were elevated for many years; about 2 years before death, ultrasound and CT showed focal changes in the liver which were later seen to be progressive. The hyperechogenicity at ultrasound and hypodensity at CT were probably due to the fatty content of the lesions which previous biopsy had shown to be histiocytosis X.

REFERENCES

ANDERSON, W. A. D. & SCOTTI, T. M., 1972. Reticuloendothelial system, spleen, and lymph nodes. In *Synopsis of Pathology*, 8th edit. (C. V. Mosby Company, Saint Louis), pp. 628–674.

KELLINGHAUS, H., RAIDT, H., STEINMEIER, R., MÜLLER, K.-M., PREUSSER, P. & LOSSE, H., 1982. Histiocytosis X bei Erwachsenen. *MedWelt, 33*, 1840–1844.

LICHTENSTEIN, L., 1955. Histiocytosis X: integration of eosinophilic granuloma of bone, "Letterer-Siwe disease", and "Schuller-Christian disease" as related manifestations of a single nosologic entity. *Archives of Pathology, 56*, 84–102.

MIŠIKOVÁ, Z., ČÁP, J., FOLTINOVÁ, A., KOSTÁLOVÁ, L. & NÉMETHOVÁ, V., 1984. Our experience with childhood histiocytosis X. *Neoplasma, 31*, 697–707.

MOURAD, K., KATZ, D. & PARADINAS, F. J., 1983. Extravisceral diffuse infiltration of adult histiocytosis X demonstrated by CT. *British Journal of Radiology, 56*, 879–881.

MUSAJI, M. A. & PARSONS, C. A., 1983. Lymphographic appearance of histiocytosis X. *British Journal of Radiology, 56*, 61–62.

SUTTON, D., 1980. *A Textbook of Radiology and Imaging*, 3rd edit. (Churchill Livingstone, Edinburgh, London, Melbourne and New York).

VANEL, D., COUANET, D., PIEKARSKI, J. D. & MASSELOT, J., 1983. Radiological findings in 23 pediatric cases of malignant histiocytosis. *European Journal of Radiology, 3*, 60–62.

VON RENNER, M., 1975. Lymphographisches Bild bei Histiozytose X. *Fortschritte auf dem Gebiete der Röntgenstrahlen, 122*, 275–276.

WOOD, C., WOOD, G. S., DENEAU, D. G., OSEROFF, A., BECKSTEAD, J. H. & MALIN, J., 1984. Malignant histiocytosis X. Report of a rapidly fatal case in an elderly man. *Cancer, 54*, 347–352.

Book reviews

Cranial Computed Tomography. By A. L. Williams and V. M. Haughton, pp. xiii + 623 + index, 1985 (C. V. Mosby Co., St Louis) £85.50.
ISBN 0-8016-5604-4

Unless the publication process is rapid, there is a danger that all new texts in this rapidly expanding and changing field may end up as reference books, rarely consulted as their message and illustrations have become out of date. The authors of *Cranial Computed Tomography*, a comprehensive text, state their objectives as producing "an authoritative up to date discussion of CT . . . pertinent to state-of-the-art CT scanners".

The book is written by two eminent neuroradiologists with the assistance of three collaborators for chapters on the posterior fossa, sella and juxta-sellar region, temporal bone and orbits. Despite there being a number of contributors, there is no contradiction in style and the text is well written, clear and concise. Radiologists and clinicians in training, as well as experienced radiologists, will find this an excellent book for day to day use as well as for reference.

Chapters are organised into clinical indications and anatomical localisation of disease, an approach which the reviewer found somewhat cumbersome and which may cause an inexperienced reader some difficulty in finding information. This, however, is a minor criticism.

The text succeeds in its aims, the illustrations are well chosen and the quality of reproduction is excellent. The abnormalities are clearly shown by arrows and illustration captions are concise and instructive.

There are excellent chapters on scanning techniques, the sella and the neonatal brain. Each chapter has a comprehensive list of fairly up-to-date references which, owing to publishing deadlines, are not as recent as one would wish. Nevertheless, it is very useful, reasonably priced, and can be highly recommended.

W. ST C. FORBES

Computed Tomography and Magnetic Resonance Imaging of the Head and Neck, 2nd edit. By Anthony A. Mancuso and William N. Hanafee, pp. 503, 1986 (Williams and Wilkins, Baltimore), £68.
ISBN 0-683-05476-7

Since the first edition of this book was published in 1982, nuclear magnetic resonance has assumed an important role in head and neck diagnosis and the authors have responded very well to this change in emphasis.

The main contribution of the book is an annotated atlas of beautifully produced and accurately labelled computed tomography and nuclear magnetic resonance scans. It is supplemented by a concise, well written text, with good, mainly anatomical diagrams, which emphasises those features of significance for radiological imaging and maintains clinical orientation and perspective. Though not comprehensive, all the important ear, nose and throat (ENT) conditions are included and there is a good index. The book is excellent value for the money and is strongly recommended for inclusion in the libraries of all departments performing ENT imaging and to trainees in the subject, especially those studying for the F.R.C.R.

BRIAN KENDALL

1986, *The British Journal of Radiology*, 59, 1127–1128 NOVEMBER 1986

Case of the month

The teenager's swollen neck

By A. C. Robinson, M.B., B.S., F.R.C.S., R. Dick, F.R.A.C.R., F.R.C.R. and G. Radcliffe, M.B., B.S., F.R.C.S.

Departments of Otolaryngology and Radiology, The Royal Free Hospital, Hampstead, London NW3 2QG

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A 13-year-old girl presented with a history of left-sided neck swelling since birth. The swelling fluctuated in size and enlarged on Valsalva manoeuvre and straining. Six weeks prior to presentation she developed tenderness and persistent swelling below the angle of the left mandible. Examination revealed a soft, fluctuant, mobile, non-pulsatile mass in that region (Fig. 1).

Plain radiography and tomography of the neck and larynx were unhelpful. Computed tomography (CT) revealed a cystic mass, with some peripheral enhancement following intravenous contrast medium, lying postero-lateral to the lower border of the mandible and lateral to the hyoid bone (Fig. 2). Aspiration of the cyst revealed dark blood, and injection of contrast medium into the cyst showed slow clearing from the lesion (Fig. 3). Common carotid arteriography showed no evidence of a chemodectoma.

What is the differential diagnosis of the lesion and how would you investigate it further?

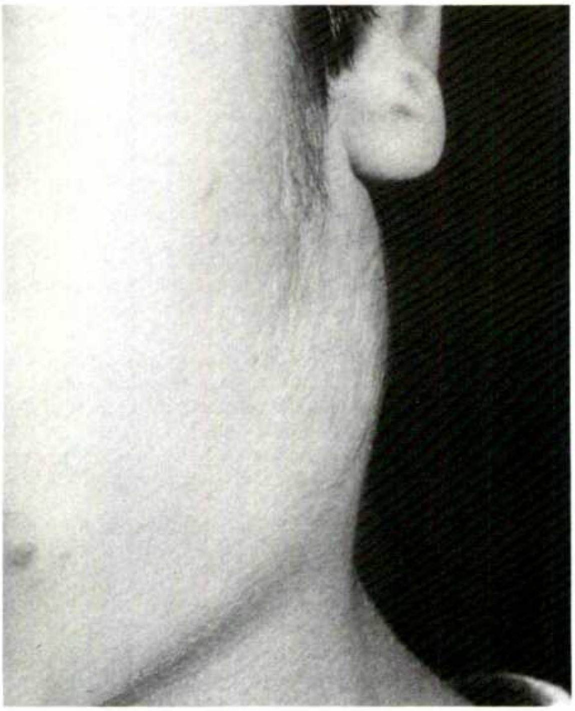

FIG. 1.

Left-sided neck mass.

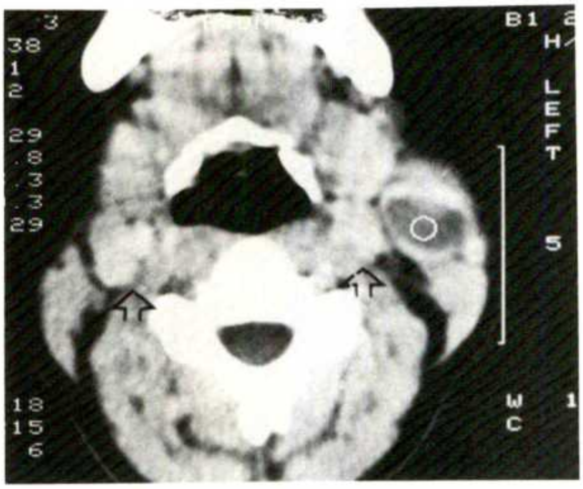

FIG. 2.

A contrast-medium-enhanced CT scan of the neck at the level of the hyoid bone. A 2 cm-diameter low-density mass lies anterior to the sterno-mastoid. The density reading suggests that part of it may be semisolid. Arrows indicate the carotid arteries and internal jugular veins. On the left side these are clearly delineated from the mass. Vascular enhancement of the wall is noted.

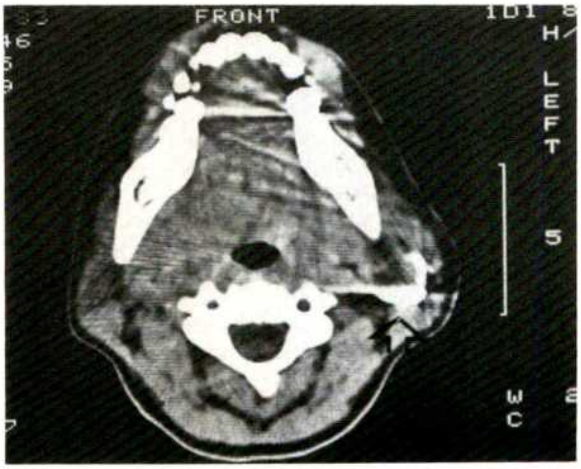

FIG. 3.

Injected contrast medium outlines the posterior wall of the lesion, and "layers" posteriorly.

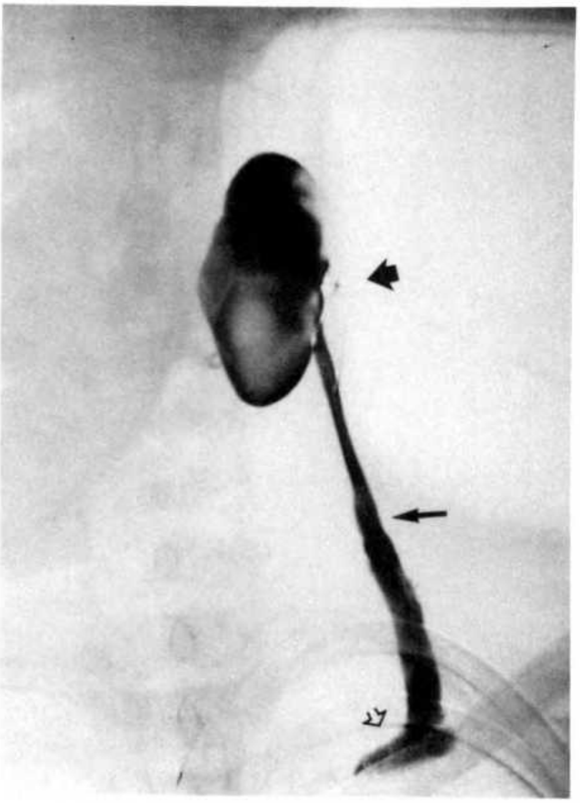

Fig. 4.

Subtraction venogram following direct injection of cyst (thick arrow). Poor mixing of contrast medium in the lower half of the cyst suggested thrombus. The thin arrow indicates the left external jugular vein and the open arrow the junction with the left subclavian vein.

Direct injection of the cystic mass was performed under fluoroscopy, and this showed a 2 cm-diameter smooth aneurysm arising from the external jugular vein (Fig. 4), and draining into the left subclavian vein.

Percutaneous embolisation was considered, but it was thought that this might result in the soft fluctuant mass being replaced by a firm one. Surgery was therefore undertaken, and confirmed an aneurysm of the external jugular vein which was being fed by the common facial and retromandibular veins. These were ligated and divided, as was the external jugular vein, and the aneurysm was removed.

The differential diagnosis of a swelling in the neck of a young person includes lymph nodes, salivary gland, cystic hygroma, branchial cyst, laryngocoele and chemodectoma. In the case presented, distension during Valsalva manoeuvre suggested that the diagnosis was more likely to be a venous aneurysm or a laryngocoele.

The true nature of the swelling was determined firstly on CT by the peripheral enhancement of the dilatation from its rich supply of vasa vasorum in the wall, secondly by the continuous aspiration of dark venous blood from the swelling, and thirdly from the convincing angiographic findings. Three treatment options were considered: surgery, sclerotherapy via an injection directly into the aneurysm and sclerotherapy via catheterisation of the external jugular vein using an occlusion balloon catheter to empty the aneurysm first. It was decided that surgery would provide the most effective method of complete cure and a good restoration of the patient's appearance was achieved. It is quite possible that with a smaller venous aneurysm one of the other treatment options may have been preferred.

Congenital dilatation of the veins of the superior vena caval system, first described by Harris in 1928, is rare, and has continued to pose a diagnostic challenge.

Various techniques have been used for diagnosis. These have included angiography (Passariello et al, 1979), direct venography (Zorn et al, 1981), and ultrasonography (Leung et al, 1983, Stevens et al, 1982). While ultrasonography has the advantage of being non-invasive, its reliability is operator-dependent and therefore a combination of techniques may produce more accurate information concerning the nature and anatomical site of the lesion.

Acknowledgment

We thank Mr John Groves, Consultant Otolaryngologist, for the opportunity to present his case.

REFERENCES

Harris, R. I., 1928. Congenital venous cyst of the mediastinum. *Annals of Surgery*, *88*, 953.

Leung, A., Hampson, S. J., Singh, M. F. & Carr, D., 1983. Ultrasonic diagnosis of bilateral congenital internal jugular venous aneurysms. *British Journal of Radiology*, *56*, 588–591.

Passariello, R., Cozzi, F., Casalena, G., Colarossi, G., Ross, P. & Simonetti, G., 1979. Angiographic diagnosis of jugular venous system dilatation in children: a report of five cases. *Pediatric Radiology*, *8*, 247–250.

Stevens, R. K., Fried, A. M. & Hood, T. R., 1982. Ultrasonic diagnosis of jugular venous aneurysm. *Journal of Clinical Ultrasound*, *10*, 85–87.

Zorn, W. G. W., Zorn, T. T. & Van Bellen, B., 1981. Aneurysm of the anterior jugular vein. *Journal of Cardiovascular Surgery*, *22*, 546–549.

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Short communications

On minimisation of toxicity to skin during capacitive radio-frequency hyperthermia

By N. M. S. Reddy, Ph.D., V. Shanta, M.D. and S. Krishnamurthi, M.S.

Cancer Institute (WIA), Adyar, Madras 600 020, India

(*Received April 1986*)

Common techniques to induce tissue hyperthermia (HT) with radio-frequency (RF) currents are either capacitive or inductive in type (Cheung, 1982, Cosset et al, 1983). An advantage with RF capacitive HT is the possibility of heating deep-seated tissues (Cheung, 1982; U et al, 1984) However, during capacitive heating the higher resistivity of subcutaneous tissues results in excessive heating, which leads to skin and fat burns and induration (Arcangeli et al, 1983, Perez et al, 1983; Hiraoka et al, 1984; Oleson et al, 1984; U et al, 1984) To prevent the direct contact of the electrode with the skin, electrodes are enclosed in bolus bags through which cooled fluids such as saline (Brezovich et al, 1981; Cheung, 1982) or deionised water (Hiraoka et al, 1984; Prionas & Hahn, 1984; U et al, 1984) are circulated Brezovich et al (1981) have shown that the skin burns during RF capacitive heating could be reduced by using a saline bolus of tissue-equivalent conductivity and Griffiths et al (1984) have reported that the extent of RF power deposition in the tissues depends on the conductivity of the bolus Here we report clinical data which, in addition to confirming the observations of Brezovich et al (1981), indicate that the excessive heating of subcutaneous fat could be reduced by cooling through the bolus and that a poorly conductive bolus should not be used during capacitive heating.

We used a "Thermotron RF 8", a capacitive 8 MHz hyperthermia unit (Yamamoto Vinyter Co), to induce tissue hyperthermia (U et al, 1984) Thermometry was carried out using copper–constantan thermocouples (IT-18, Sensortek), which were implanted in the tissue at the desired depths using hypodermic needles Figure 1 indicates the electrode positions during the treatment of cheek carcinomas Details of the tumours treated and the treatment protocol are given in Table I At the start of the clinical trials we used 0.1% saline in the electrode–skin cooling system, as per the recommendations of the manufacturer. Three of the first 10 patients suffered from first and second degree burns at sites corresponding to the bolus edges A skin erythema was not uncommon. There was also the spread of RF currents throughout the surface of the body of the patient, which resulted in mild (low kV) to severe (high kV) shock to the patient and to the attending personnel on loose contact and the sensation of heating on firm contact When we used 1.0% saline bolus the skin burns, skin erythema and the spread of RF currents on the body surface were minimised as shown in Table I

The use of 1 0% saline was based on our observation that the rate of heating of agar phantoms of 21.0 cm diameter and 10 cm height (4.0% agar, 0.22% NaCl, 0.1% sodium azide and 95.68% deionised water, with 0 6 S/m conductivity heated with a pair of 10 cm-diameter electrodes) was a maximum when the saline concentration in the bolus was 1 0%. The ratio of the rate of heating of phantom to that of bolus for 0 05%, 0.45%, 1 0% and 1 5% saline in the bolus was 0 17, 0.93, 1.25 and 1.22, respectively These data indicate that 1.0% saline bolus maximises and evens out the power deposition in the tissues and reduces the concentration of RF field lines in the bolus and the associated hot spots consequent upon the geometrical discontinuity between the tissue and the electrode when the low conductivity bolus is used. In addition to the use of 1.0% saline bolus with uniform circulation, even distribution of the bolus around the electrode and between the skin and the electrode, as shown in Fig. 1, was found to reduce the number of hot spots further and to minimise the skin toxicity.

Figure 2 indicates that the overheating of subcutaneous fat could be minimised by cooling through the bolus These data were recorded when a tumour in the left retroperitoneal region of an obese patient was heated using 14 cm- and 10 cm-diameter electrodes mounted on the left lumbar and retroperitoneal regions, respectively. During other HT treatments we have also noted that the temperature of adipose tissue at 0 5 cm could be maintained below 40 0°C and the temperature at 2 cm could be brought down to that of the tumour with differential cooling of the boluses, *i e* cooling the bolus close to the fatty tissue to less than 15°C and maintaining the temperature of the bolus close to the tumour around 40.0°C

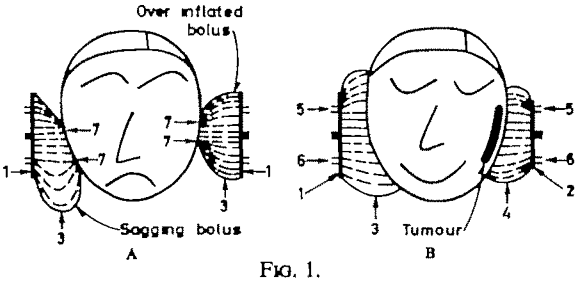

FIG. 1.

Schematic sketch of the frontal view of (A) an incorrect and (B) a correct setting of boluses during RF heating. 1 = 10 cm-diameter electrodes, 2 = 8 cm-diameter electrode, 3 = 16 cm-diameter boluses, 4 = 12 cm-diameter bolus, 5 = saline inlet, 6 = saline outlet, 7 = hot spots due to higher RF current density. Dashed lines in boluses represent path of RF currents.

Address for reprints: N. M. S. Reddy, Department of Radiation Oncology, Box 1212, SUNY, Health Science Center, 450 Clarkson Avenue, Brooklyn, NY 11203, USA

TABLE I

TREATMENT PROTOCOL AND THE ASSOCIATED TOXICITY

Percentage of saline in the bolus	Tumour histology, site and length (cm)	No. of patients	No of HT treatments per patient 30–60 min per treatment	Average temperature (°C)		Average power (W)†		Toxicity			
				Skin*	Tumour	Forward	Reflected	Current spread on the skin surface	Skin erythema	Skin burns	Induration of subcutaneous tissues
0 1	Carcinoma, cheek 5–8	10	16	30.0	41.5	600	30	Yes	Yes	Yes‡	Yes
1.0	Carcinoma, cheek 5–8	25	16	15.0	41.5	250	0–5	Nil	Nil	Nil	Reduced
1 0	Sarcomas, various sites 4–20	20	12–16	15 0	43 0	200–400	0–40	Nil	Nil	Nil	Reduced

*With 1% saline bolus the skin temperature could be raised to above 42.0°C without causing skin burns, when the skin also was involved.

†Forward power and reflected power varied with the anatomical site, size and combination of electrodes, weight of the patient, etc

‡Two female and one male patient suffered from skin burns on the upper cheek, the back of the external earlobe and the lateral sides of the neck

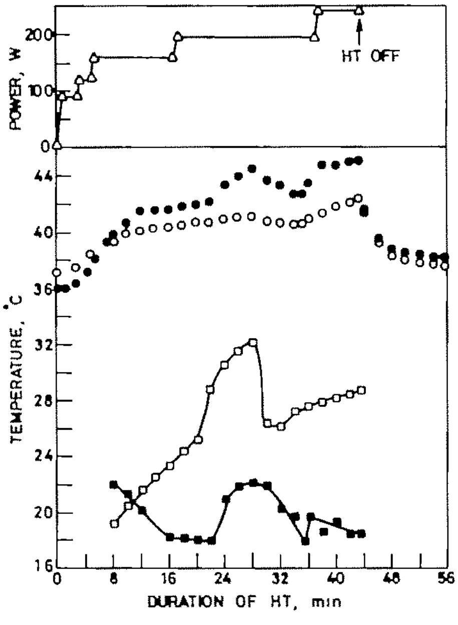

FIG. 2

Effect of cooling of the bolus on the temperature of tissues below the bolus during RF capacitive HT ● temperature of fat (left lumbar region) below bolus A at 1 5 cm depth; ■ temperature of bolus A; ○ temperature of the tumour below bolus B (left retroperitoneal region) at a depth of 1.85 cm; □ temperature of bolus B; △ absorbed power (W)

In conclusion, it is possible to say that the use of well cooled 1% saline bolus would minimise the absorption of RF power in the circulating fluid, even out the power deposition in the tissues and minimise the toxicity to skin and fat during RF capacitive heating.

ACKNOWLEDGMENTS

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REFERENCES

ARCANGELI, G, CIVIDALLI, A, LOVISOLO, G & NERVI, C., 1983. Clinical results after different protocols of combined local heat and radiation *Strahlentherapie, 159*, 82–89

BREZOVICH, I A, LILLY, M B., DURANT, J. R. & RICHARDS, D B., 1981. A practical clinical system for clinical radiofrequency hyperthermia. *International Journal of Radiation Oncology, Biology, Physics, 7*, 423–430.

CHEUNG, A Y., 1982. Microwaves and radiofrequency techniques for clinical hyperthermia. *British Journal of Cancer, 45*, Suppl. V, 16–21.

COSSET, J. M, DUTREIX, J & FARIA, S., 1983. Technical basis for the application of localized hyperthermia. *Strahlentherapie, 159*, 315–318

GRIFFITHS, H., AHMED, A. & SMITH, C. W., 1984. Power loss in skin cooling pillows during RF hyperthermia. *British Journal of Radiology, 57*, 254–256

HIRAOKA, M., JO, S.. DODO, Y, ONO, K., TAKAHASHI, M, NISHIDA, H. & ABE, M., 1984. Clinical results of radiofrequency hyperthermia combined with radiation in the treatment of radioresistant cancers *Cancer, 54*, 2898–2904.

Short communications

OLESON, J. R., MANNING, M. R., SIM, D. A., HEUSINKVELD, R. S., ARISTIZABAL, S. A., CETAS, T. C., HEVEZI, J. M. & CONNOR, W. G., 1984. A review of the university of Arizona human clinical hyperthermia experience. In *Frontiers of Radiation Therapy and Oncology*, Vol. 18. Ed. by J. M. Vaeth (Karger, Basel), pp. 136–143.

PEREZ, C. A., NUSSBAUM, G., EMAMI, B. & VONGERICHTEN, D., 1983. Clinical results of irradiation combined with local hyperthermia. *Cancer*, *52*, 1597–1603.

PRIONAS, S. D. & HAHN, G. M., 1984. Temperature distributions induced in pig tissues by a water-cooled disk electrode RF system. *Medical Physics*, *11*, 22–25.

U, R., HIRAOKA, M., TAKAHASHI, M., ABE, M., MATSUDA, T., SUGIYAMA, A., NAKADA, Y., YAMAMOTO, I. & SUGAHARA, T., 1984. Thermoradiotherapy of refractory malignant tumours: an experience with microwave and RF capacitive hyperthermia. *Medical Instrumentation*, *18*, 181–186.

Physical and biological dosimetry at the barium sulphate–culture medium interface

By N. Tokita, I. van der Kogel, *J. J. Chmielewski and M. R. Raju

Life Sciences and *Physics Divisions, Los Alamos National Laboratory, University of California, Los Alamos, NM 87545, USA

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Barium sulphate suspensions (BSS) used in gastrointestinal radiography consist of barium sulphate microparticles which coat the mucosal surface of the digestive tract. The amount of BSS which adheres to the mucosa depends upon the procedure employed, the type of BSS, the amount and dilutions used, and the surface properties of the mucosa (Gelfand & Ott, 1982). These barium microparticles, once taken internally, penetrate deeply into the intestinal mucosa, even into the crypts between villi (Simmonds & James, 1976), forming tissue–barium interfaces. An interface between a solid metal and a tissue when irradiated yields a region of overdosage at the proximal interface and an underdosed region at the distal side (Dutreix & Bernard, 1966). However, suspended barium (atomic number (Z) = 56) microparticles release secondary electrons in all directions when irradiated, resulting in overdosage regions on both sides of the interface. In this communication, we report the measurement of doses at regions proximal and distal to a culture medium–BSS interface by a biological assay (cell survival) method, as a simulation of the dosimetry at the tissue–BSS interface. Physical dosimetry was also carried out to measure the amount of secondary electrons released from BSS and from a mylar membrane.

METHODS

A 250 kVp X-ray unit (GE Maxitron, filtered with Thoraeus II, 3 mm Cu half value layer) was used since this was the only radiation source available in our laboratory. The focus–skin distance was 31 cm with no collimator attached to the X-ray window. Radiation exposures and absorbed doses were measured using a Victoreen chamber and a semiconductor dosemeter. An extrapolation chamber (G5-TG, EG & G) was used to measure secondary electrons released at the distal surface of a 1.5 μm-thick mylar membrane (Du Pont) on which a thin layer of 60% w/v BSS (55 mg/cm^2, Picker RapidFil barium pack) was placed. The window of the chamber consisted of 50 μg/cm^2 polyhydrocarbon coated with 50×10^{-10} m Nichrome. Its physical configuration limited the use of the chamber only at the distal surface of the mylar.

The mylar dish used for biological assay consisted of a 3.5 cm-diameter glass ring covered with a mylar membrane as described elsewhere (Barendsen & Breusker, 1960; Goodhead & Thacker, 1977). Asynchronously growing Chinese hamster (V79) cells were plated into mylar dishes at a density of 10^5 cells/dish in 2.5 ml of alpha MEM medium supplemented with 10% fetal calf serum (Rehatuin). After a 48 h incubation period, to allow cell adhesion and flattening without reaching confluency, medium was added to make the depth of medium 1 cm. The dish was placed on a 1 cm-thick polystyrene plate with an appropriate amount of an interface material, for example, BSS or water, in between the dish and the plate (Fig. 1). The dish/polystyrene plate was then suspended in air by a pair of laterally extending plastic arms. The set-up provided the same amount of "tissue-equivalent material" (1 cm-thick medium and polystyrene) on both sides of the monolayered cells. A small amount of BSS or water was spread inside a 3.5 cm-diameter O-ring attached to the polystyrene plate and covered with a mylar membrane with no air gap allowed between the under-surface of the mylar dish and the BSS. The cells were irradiated either from above or below at an exposure rate of 5×10^{-1}C kg^{-1} min^{-1} at room temperature.

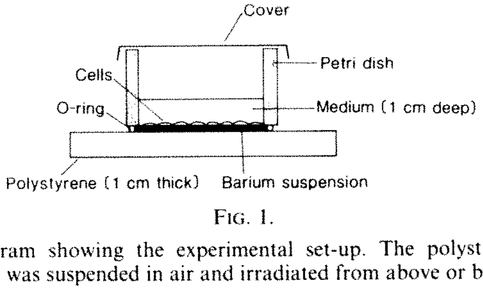


FIG. 1.

Diagram showing the experimental set-up. The polystyrene plate was suspended in air and irradiated from above or below.

Address for correspondence: Dr M. R. Raju, Mail Stop M880, Los Alamos National Laboratory, Los Alamos, NM 87545, USA.

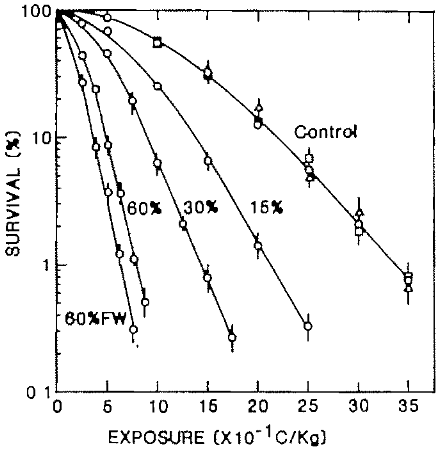


FIG. 2.

Cell survival plotted as a function of exposure. Control: cells on mylar placed on a 0.27 mm-thick layer of water exposed from above (○) and from below (□); cells on polystyrene Petri dishes placed on a 0.27 mm-thick layer of 60% w/v BSS (△) Survival at the proximal interface· cells on mylar on 0.27 mm-thick BSS at 60%, 30% and 15% w/v Survival at the distal interface. cells on mylar on a 0.27 mm-thick layer of 60% w/v BSS exposed from below (60% FW) Data obtained from minimum of three separate experiments for each data point. Error bars show SEM

One may choose any thickness of BSS as an interface medium; however, our primary interest was to compare the results obtained from *in-vitro* and *in-vivo* studies under the same circumstances Therefore, we derived the thickness of BSS used in this assay from an *in-vivo* study Mice (Balb/c male, 24 weeks old) were not fed but given water *ad libitum* for 14 h and then 0.5 ml of standard 60% w/v BSS was introduced directly into the stomach through a gastric feeding tube under ethrane anaesthesia. Radiographs revealed that the BSS had filled the jejunum approximately 1 h after feeding. Six mice were sacrificed and the upper jejunum clamped, removed and processed immediately to obtain frozen sections The average thickness of the BSS, measured microscopically, was in the range 0.25–0 3 mm. We therefore used a 0.27 mm-thick layer of BSS for this study. Various dilutions of BSS (60% to 1 9% w/v) were also used to measure the effect of barium sulphate density on the interface dose. Water was used as a control.

When the dish on the polystyrene plate was irradiated from above, the cells on mylar membrane (located between the culture medium and the BSS layer) were used for dosimetry at the region proximal to the medium–BSS interface. Under the same set-up, the cells irradiated from below were used for dosimetry at the distal surface of the BSS–medium interface. After irradiation, the cells were trypsinised and counted, and aliquots of the cells were plated into plastic Petri dishes for colony formation to obtain cell survival A similar study was also carried out using cells plated in polystyrene Petri dishes (0.6 mm-thick, 35 mm in diameter, Falcon) For this study, 2×10^4 cells/dish were plated 48 h before irradiation

Cell survival data were analysed using a fitting program based on the model $S=\exp(-aX-bX^2)$, where S is the survival and X the exposure (C kg^{-1}).

RESULTS AND DISCUSSION

Physical dosimetry based on the extrapolation chamber indicated that the chamber current increased by 35% when the mylar was placed directly on the window compared with the reading taken when the chamber was suspended in air. When a 0.27 mm-thick layer of BSS (60% w/v) was placed on the mylar and measured directly at the under-surface of the mylar, the current increased by a factor of 6 9 These data indicate that the presence of the BSS layer increased exposure 5 6-fold at its distal surface after correcting for the effect of the mylar

The cell survival data used for biological dosimetry are shown in Fig. 2 As an exposure control, cells were plated on mylar or on polystyrene Petri dishes, placed on a thin layer of water attached to the polystyrene plate and irradiated from above or below The cell survival as a function of exposure was similar under each of these conditions. In addition, the survival curve for cells plated on polystyrene Petri dishes and irradiated on a 0 27 mm-thick layer of BSS (60% w/v) was the same as for the control, indicating that secondary electrons released from BSS are unable to penetrate 0.6 mm polystyrene.

In contrast, survival curves of cells attached to mylar on a 0 27 mm-thick layer of BSS have considerably steeper slopes than the control curves, depending upon the density of BSS After fitting the data using a linear-quadratic model, the exposure ratios were compared at 50%, 10% and 1% survival levels as shown in Table I Exposure ratio, defined as the exposure for control divided by the exposure for a given barium dilution, was used to estimate the dose increase at the interface This value varies depending upon the barium density and the survival level as an end-point. The presence of a 0 27 mm-thick layer of BSS (60% w/v) increased the exposure at the proximal interface by a factor of 4.4 at the 10% survival level. With the same experimental set-up, but irradiating from below the cells to determine the distal interface dose, the slope of the survival curve was slightly steeper, with an exposure ratio of 5.8 measured at the 10% survival level The latter is in agreement with the physical dosimetry data The differences in exposure ratio at three survival levels (Table I) may result from the fact that cells located at the edge of the mylar dish may receive fewer secondary electrons and that some cells "piggy-back" without attaching directly to the mylar, even at a low cell density. Figure 3 shows the dose increase calculated from the exposure ratio at the proximal interface plotted as a function of barium density measured at 10% survival levels The dose was reduced as the BSS was diluted, reaching the control (water) level at, approximately, a 1/8 dilution, or 7 5% w/v.

These results with BSS differ from previously studied metal–tissue interface effects in which there are regions of "build-up" and underdosage across the interface (Dutreix & Bernard, 1966). Dosimetry has been reported previously for bone–tissue interfaces with X rays (Spiers, 1949), copper–tissue interfaces in a ^{60}Co γ-ray beam (Dutreix & Bernard, 1966), metal–tissue interfaces in high-energy electron beams (Okumura et al, 1971, Saunders & Peters, 1974), and gold-and-amalgam–tissue interfaces during exposure to 4–6 MeV photons (Gibbs et al, 1976) The metal–tissue interface may pose a clinical problem of enhanced normal-tissue damage during therapeutic irradiation (Gibbs et al, 1976) At photon energies of 10–20 MeV, the soft tissues are always overdosed when in contact with a high-atomic-number material, regardless of the direction of the radiation, depending upon the Z number and the energy (Dutreix &

TABLE I

Cell survival coefficients (a, b) and exposure values at three survival levels for control (water) and three different BSS densities as an interface medium

Interface medium	a ($\times 10^{-2}$ /C kg^{-1})	b ($\times 10^{-3}$ /C^2 kg^{-2})	50% survival exposure (C kg^{-1})	ratio	10% survival exposure (C kg^{-1})	ratio	1% survival exposure (C kg^{-1})	ratio
Water	3.37	3.43	10.1	1.0	21.5	1.0	32.1	1.0
15% Ba (p)	7.55	6.47	5.98	1.69	13.7	1.57	21.1	1.52
30% Ba (p)	10.8	15.4	4.06	2.50	9.22	2.33	14.1	2.27
60% Ba (p)	26.2	43.5	1.99	5.09	4.87	4.41	7.71	4.16
60% Ba (d)	46.9	40.9	1.32	7.65	3.71	5.79	6.32	5.07

Ratio = exposure for water/exposure for Ba; (p) = exposure at the proximal interface; (d) = exposure at the distal interface.

Bernard, 1966). It remains to be evaluated whether the BSS–tissue interface effect poses a problem of enhanced intestinal morbidity during irradiation with high-energy photons and/or with lower-energy γ-rays often used in brachytherapy. Our calculations, however, predict that the BSS–tissue interface effect is not likely to be significant for 662 keV γ rays from ^{137}Cs, a commonly used radionuclide in brachytherapy. Experimental *in-vitro* and *in-vivo* studies are in progress to evaluate the interface effect using high-energy photons and electrons (4–20 MeV) and low-energy X rays (50–100 kVp) used in diagnostic radiography.

In summary, the present study suggests that a thin layer of BSS forms an interface with tissues which results in high dose regions on both sides of the BSS–tissue interface when irradiated with 250 kVp X rays. The magnitude of dose increase depends on the density of BSS.

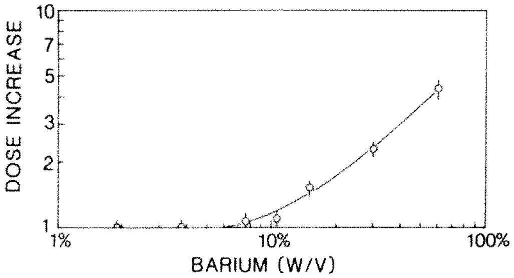


Fig. 3.

Dose increase calculated from the exposure ratio (the exposure for control/the exposure for a given barium dilution) at the proximal interface plotted as a function of BSS density calculated at the 10% survival level. The exposure reached the control (water) level at 7.5% w/v BSS.

Acknowledgments

The authors are grateful to James P. Freyer and Anita P. Stevenson for their comments and advice. This work was supported in part by a grant CA 37269 awarded by the National Cancer Institute, USDHW and by the Department of Energy.

REFERENCES

Barendsen, G. W. & Breusker, T. L. J., 1960. Effects of different ionizing radiations on human cells in tissue culture: I. Irradiation techniques and dosimetry. *Radiation Research, 13*, 823–840.

Dutreix, J. & Bernard, M., 1966. Dosimetry at interfaces for high energy x and gamma rays. *British Journal of Radiology, 39*, 205–210.

Gelfand, D. W. & Ott, D. J., 1982. Barium sulfate suspensions: an evaluation of available products. *American Journal of Roentgenology, 138*, 935–941.

Gibbs, F. A., Jr, Palos, B. & Goffinet, D. R., 1976. The metal/tissue interface effect in irradiation of the oral cavity. *Radiology, 119*, 705–707.

Goodhead, D. T. & Thacker, J., 1977. Inactivation and mutation of cultured mammalian cells by aluminium characteristic ultrasoft X-rays. I. Properties of aluminium X-rays and preliminary experiments with Chinese hamster cells. *International Journal of Radiation Biology, 31*, 541–559.

Okumura, Y., Mori, T. & Kitagawa, T., 1971. Modification of dose distribution in high-energy electron beam treatment. *Radiology, 99*, 683–686.

Saunders, J. E. & Peters, V. G., 1974. Back-scattering from metals in superficial therapy with high energy electrons. *British Journal of Radiology, 47*, 467–470.

Simmonds, R. & James, A. M., 1976. An *in vitro* investigation of barium meals. *Cytobios, 15*, 191–200.

Spiers, F. W., 1949. The influence of energy absorption and electron range on dosage in irradiated bone. *British Journal of Radiology, 22*, 521–533.

Book review

Atlas of Clinical Rheumatology. By P. Dieppe, P Bacon, A Bamji and I. Watt, pp. 364, 1986 (Oxford University Press, Oxford), £75.00
ISBN 0–906923–75–1

Teachers of clinical rheumatology have the great advantage that so much of the effect of most rheumatic disorders is visible at the bedside or detectable by simple clinical manoeuvres. It is a logical step, therefore, to bring together in atlas form the common and not so common manifestations of joint and other connective-tissue disorders The authors have, by and large, carried out this task admirably Introductory sections describe the range of physical signs encountered and the various methods of investigation available. The disease groups are then dealt with in a comprehensive fashion, section by section, and the overall standard of illustration is excellent.

This atlas does not confine itself to superficial appearances but, wherever relevant, includes excellent radiographs and histological sections, with very useful line drawings guiding the reader to the corresponding salient features. There is an occasional slip, *e.g.* the appearance of the tongue chosen to illustrate the xerostoma of Sjögren's syndrome is not at all characteristic. The illustration of the various appearances of synovial effusions does not include a good example of the commonest, the pale yellow fluid aspirated from joints with the common inflammatory arthropathies. Those readers who have difficulty with the concept of mixed connective-tissue disease are unlikely to be convinced about its validity on the basis of the illustrations.

Enough supportive text is provided to supply a theoretical framework for the material illustrated. In reproducing in diagram form a scheme relating certain types of vasculitis and granulomatous conditions, the mistaken idea that midline granuloma is part of this spectrum of conditions is, unfortunately, repeated.

The authors and publishers are to be congratulated on the high standard of this volume, which is highly recommended and which should find a place in any undergraduate or postgraduate medical library. Radiologists should find it a considerable help in relating the radiographic appearances they encounter with the corresponding clinical and pathological changes.

J C WOODROW

1986, *The British Journal of Radiology*, 59, 1135–1136 NOVEMBER 1986

Correspondence

(The Editors do not hold themselves responsible for opinions expressed by correspondents)

"Invisible" field skin marking on radiotherapy patients

THE EDITOR—SIR,

Radiotherapy skin marks, especially those marks on exposed areas such as the face, cause many patients to be understandably self-conscious and embarrassed when in public. There is a need for an alternative to the gentian violet skin marking method generally used in radiotherapy. A simple but effective answer to the problem is to use a marking which is invisible in ordinary light but visible on the treatment machine.

A skin marker is used which is visible only in the ultra-violet (UV) range, commonly known as "black light". In the simulator and treatment rooms there are fitted, in place of the dim lights, two UV lamps, one either side of the couch. Any marks present or being applied can be clearly seen, thus enabling the treatment to be set up normally. The ink used does not appear to have any toxic effect on tissue and when dry does not remove easily, although isopropyl alcohol injection swabs will remove any unwanted marks. The pens are normally used for security marking and are marketed by Berol and are known as the "Berol Detective". The UV lamps are ordinary bayonet-cap fitting and can be used as a direct plug-in replacement for a tungsten lamp. The Thorn MBWT/V, a high-pressure mercury discharge in a quartz arc tube, is suitable. The bulb is of black glass, which absorbs virtually all radiation other than that in the long-wave UV of predominantly 365 nm. Little visible light is emitted.

Yours, etc.,
R. E. HUTCHINGS

Department of Medical Physics,
Norfolk & Norwich Hospital,
Brunswick Road,
Norwich NR1 3SR

(*Received July 1986*)

Measurement of lung water using nuclear magnetic resonance imaging

THE EDITOR—SIR,

In their recent paper describing the regional measurement of lung water using nuclear magnetic resonance (NMR) imaging, MacLennan et al (1986) fail to discuss adequately two important issues. In the introduction, they quote a number of alternative techniques to measure this parameter, but conclude that none is ideal, either for the monitoring of treatment or for use as a research tool. Unfortunately, the authors do not discuss the merits or demerits of these alternative techniques, in spite of the fact that a number of different approaches to measuring lung water have been made using positron emission tomography (PET), which have been shown to be able to provide accurate values of regional lung density (g lung/ml thorax), regional water density (ml water/ml thorax), regional extravascular density (g tissue/ml thorax) and regional blood volume (ml blood/ml thorax). Although PET may not yet be freely available (there are currently 20–30 working PET centres throughout the world), it has been shown to be a powerful research tool—as testified by a number of clinically important research studies based on the measurement of lung water (Wollmer et al, 1983, 1984a, b; Schober et al, 1985).

TABLE I

	Subject	Reference
Lung density (g/ml)		
0.24	Dog, supine	Gamsu et al (1979)
0.32	Man, sitting	Garnett et al (1977)
0.30	Man, supine	Unpublished data
0.29	Man, supine	Rhodes et al (1981)
Lung water density (ml/ml)		
0.31	Man, supine	Schober et al (1985)
0.27	Dog, supine	Schuster et al (1985)

The second point arises from the extremely low values of lung water density reported by this group. Table I documents values obtained by a number of workers using a wide range of techniques both in man and the dog. This would suggest a value for lung density of 0.30 g/ml thorax, typical of the right lung/caudal slice in the supine posture. This value translates into a value for water density of 0.26 ml/ml thorax (assuming a lung (tissue + blood) water content of 0.85 ml/g) and suggests that values obtained using NMR imaging (0.16 ml water/ml thorax, caudal plane/right lung slice) underestimate the true water density by nearly 40%. The large difference between their measurements of water or tissue density and those in Table I is not reported and the discussion is limited to the acknowledgment of a 10% error due to insufficient relaxation time between pulsing, and a mention of the partial volume effect, which, with a 1.6 cm-thick slice, should be of minimum involvement. The implication, therefore, is that some other substantial error in the technique exists which should be investigated before this approach is relied upon to provide routine clinical measurements.

Yours, etc.,
CHRISTOPHER G RHODES

MRC Cyclotron Unit,
Hammersmith Hospital,
Ducane Road,
London W12 0HS

(*Received June 1986*)

REFERENCES

GAMSU, G., KAUFMAN, L., SWANN, S. J & BRITO, A. C., 1979. Absolute lung density in experimental canine pulmonary oedema. *Investigative Radiology, 14*, 261–269.

GARNETT, E. S., WEBB, C. E., COATES, G., COCKSHOTT, W. P., NAHMIAS, C. & LASSEN, N., 1977. Lung density: clinical method for quantitation of pulmonary congestion and oedema. *Canadian Medical Association Journal, 116,* 153–154.

MACLENNAN, F. M., FOSTER, M. A., SMITH, F. W. & CROSHER, G. A., 1986. Measurement of total lung water from nuclear magnetic resonance images. *British Journal of Radiology, 59,* 553–560.

RHODES, C. G., WOLLMER, P., FAZIO, F. & JONES, T., 1981. Quantitative measurement of regional extravascular lung density using positron emission and transmission tomography. *Journal of Computer Assisted Tomography, 5,* 783–791

SCHOBER, O. H., MEYER, G. J., BOSSALLER, C., CREUTZIG, H., LICHTLEN P. R. & HUNDESHAGEN, H., 1985. Quantitative determination of regional extravascular lung water and regional blood volume in congestive heart failure. *European Journal of Nuclear Medicine, 10,* 17–24.

SCHUSTER, D. P., MINTUN, M. A., GREEN, M. A. & TER-POGOSSIAN, M. M., 1985. Regional lung water and hematocrit determined by positron emission tomography. *Journal of Applied Physiology, 59,* 860–868.

WOLLMER, P., RHODES, C. G., ALLAN, R. M., MASERI, A. & FAZIO, F., 1983. Regional extravascular lung density and fractional pulmonary blood volume in patients with chronic pulmonary venous hypertension. *Clinical Physiology, 3,* 241–256.

WOLLMER, P., RHODES C. G. & HUGHES, J. M. B., 1984a. Regional extravascular density and fractional blood volume of the lung in interstitial disease *Thorax, 39,* 286–293

WOLLMER, P., ROZKOVEC, A., RHODES, C. G., ALLAN, R. M. & MASERI, A., 1984b. Regional pulmonary blood volume in patients with abnormal blood pressure or flow in the pulmonary circulation *European Heart Journal, 5,* 924–931.

(*Author's reply*)

THE EDITOR—SIR,

In reply to the letter from Dr Rhodes, no criticism of PET as a research tool was intended.

The method described in our article was one possible approach to the problem of lung water measurement using magnetic resonance imaging. We emphasise repeatedly in the discussion that the method appears to underestimate lung water. In addition to the loss resulting from partial saturation and partial volume effects, we also suggested that the T_2 shortening effect of lung inflation described by Morris et al (1985) might be a significant source of signal loss using the Aberdeen saturation-recovery sequence. Unfortunately, we are not in a position to investigate this. The range of values reported for lung density is not quite as narrow as the range referred to by Dr Rhodes. Values of 0.19 ± 0.03 (1 SD) resulted from a radiographic and helium dilution method (Armstrong et al, 1982), although these subjects were sitting, not lying.

Yours, etc.,
F. M. MACLENNAN

Department of Anaesthesia,
Royal Infirmary,
Aberdeen AB9 2ZB

(*Received June 1986*)

REFERENCES

ARMSTRONG, J. D., GLUCK, E. H., CRAPO, R. O., JONES, H. A. & HUGHES, J. M. B., 1982. Lung tissue volume estimated by simultaneous radiographic and helium dilution methods. *Thorax, 37,* 676–679.

MORRIS, A. H., BLATTER, D. D., CASE, T. A., CUTILLO, A. G., AILION, D. C., DURNEY, C. H. & JOHNSON, S. A., 1985. A new nuclear magnetic resonance property of lung *Journal of Applied Physiology, 58,* 759–762

1986, *The British Journal of Radiology*, *59*, 1137–1141 NOVEMBER 1986

Proceedings of The British Institute of Radiology

Radiobiology work-in-progress

Abstracts of papers presented at the above meeting, held at 36 Portland Place, London W1N 3DG on Friday, February 21, 1986

Chairmen: Dr J. W. Hopewell and Dr S. B. Field

The biological effects of 24 keV neutrons and their relevance to neutron-capture therapy, by A. J. Mill, G. R. Morgan and C. J. Roberts.
The role of quaternary structure in the radiation sensitivity of human lymphocytes: a target identified, by W. A. Cramp and S. A. Sabovljev
High yields of lethal mutations in somatic mammalian cells that survive ionising radiation, by C. B. Seymour, C. Mothersill and T. Alper
The effects of localised pelvic irradiation in the rat: the influence of field positioning, by G. A. Ross and J. W. Hopewell
The effect of fractionated irradiation on the rat heart, by K. R. Trott and S. Lauk
The response of the mouse kidney to very low X-ray doses per fraction, by M. C. Joiner, J. Denekamp and B. D. Michael
Changes in duodenal endocrine cell population and villous structure after X irradiation, by M. G. Wyatt, S. P. Hume, K. E. Carr and J. Marigold
Influence of circadian rhythms on radiosensitivity in mouse skin, by B. Stadler, A. Rojas, J. Soranson and J. Denekamp

THE BIOLOGICAL EFFECTS OF 24 KEV NEUTRONS AND THEIR RELEVANCE TO NEUTRON-CAPTURE THERAPY

A. J. Mill, *G. R. Morgan and *C. J. Roberts

*Radiobiology Laboratory, Berkeley Nuclear Laboratories, CEGB, Berkeley and *Environmental and Medical Sciences Division, AERE, Harwell*

There is currently considerable interest in the biological effects of intermediate-energy neutrons. Firstly, in radiological protection, since a large proportion of the neutron dose received by personnel around nuclear reactors stems from this energy region. Secondly, in fundamental radiobiology, because the ranges of the protons produced by intermediate-energy neutrons are of the order of the distances thought to separate radiation-sensitive sites in mammalian cells. Thirdly, for neutron-capture therapy, since these neutrons provide a penetrating thermal-neutron profile without an excessively high recoil-proton dose. Neutron-capture therapy involves the selective uptake by a tumour of a substance (such as boron) which has a high cross-section for the capture of thermal neutrons. After exposure to neutrons, the capture products (alpha particles and lithium recoil nuclei) irradiate only the cells containing boron.

Beams of intermediate-energy neutrons may be produced by filtering the neutrons from a high-flux reactor. A filter of iron and aluminium gives 24 keV neutrons. A filter of scandium gives 2 keV neutrons. Neutron transport calculations have shown that neutrons of these energies can provide suitable beams for the treatment of gliomas by boron neutron-capture therapy (BNCT). A high-purity beam of 24 keV neutrons has recently been developed on the PLUTO reactor at AERE, Harwell. Measurements showed that the beam fluence contained $>95\%$ monoenergetic 24 keV neutrons with principal high-energy contamination at 130 and 280 keV. The neutron dose-rate was 0.18 Gy/h, plus 0.03 Gy/h of gamma radiation; 80% of the kerma was attributable to 24 keV neutrons. Plateau-phase cultures of HeLa cells (CEGB) and V79 cells (AERE) were irradiated in this beam in order to measure the relative biological effectiveness (RBE) for cell killing and for chromosome aberrations. The cultures were maintained at 37°C for the duration of the exposures, which lasted up to 24 h. Analysis of the survival data gave limiting RBE values, at low doses, of 3.7 (HeLa cells, compared to 250 kVp X rays) and 2.7 (V79 cells, compared to ^{60}Co gamma rays). The results indicated that 24 keV neutrons behave as high linear energy transfer radiation. No other survival data are available for comparison. In a more recent series of experiments, HeLa cells were irradiated at various depths in a tissue-equivalent phantom. Boron 10 was added to some of these cultures in order to assess the RBE of the alpha particles emitted after neutron capture. Preliminary data suggest that the RBE of these alpha particles is similar to that of 24 keV neutrons. Enhanced cell killing at depth for borated cells is a function of the depth-dose distribution. It is clear that intermediate-energy neutrons are superior to thermal-energy neutrons for BNCT, as currently practised in Japan.

THE ROLE OF QUATERNARY STRUCTURE IN THE RADIATION SENSITIVITY OF HUMAN LYMPHOCYTES: A TARGET IDENTIFIED

W. A. Cramp and S. A. Sabovljev

MRC Radiobiology Unit, Royal Postgraduate Medical School, Hammersmith Hospital, London W12 0HS

In mammalian cells DNA has a higher order of configuration than two interwound strands of sugar-phosphate backbones along which are positioned the purine and pyrimidine bases. As well as being wound around histone proteins, this double-stranded DNA is in close association with three other specific types of protein. These are the "lamina" proteins at the periphery of the nucleus, which are embedded in the nuclear membrane, the "matrix" proteins which run throughout the nucleus, and the "scaffold" proteins, responsible for the structure of condensed chromosomal DNA. The quaternary structure of DNA is considered to be the three-dimensional association of all these macromolecules.

The most radiation sensitive volume in mammalian cells is located at the periphery of the nucleus and may contain the nuclear membrane. At this site there is predominantly DNA in association with "lamina" proteins and it is believed that the link between double-stranded DNA and these proteins is through a copper atom.

The density of histone-free DNA-protein material isolated from human peripheral blood lymphocytes has been shown to decrease when the cells are irradiated. They return to the unirradiated density when the cells are incubated in nutrient medium. When this return to unirradiated densities was slow, it was found that radiation inhibition of cell proliferation was enhanced. This relates to a slow return to cellular radiation hypersensitivity This DNA-protein material can be made less dense by treatment of the lymphocytes or their nuclei with agents which either extract copper or modify its oxidative state. Added copper increases the density of the DNA-protein complex. The technique used determines the density characteristics of all the histone-free DNA-protein complexes, not solely the DNA associated with the "lamina" proteins found at the nuclear periphery However, it has been deduced that the radiation sensitivity of lymphocytes is dependent upon the cells' ability, in instances such as in old and diseased donors, the much reduced ability, to restore the correct copper-protein configuration.

HIGH YIELDS OF LETHAL MUTATIONS IN SOMATIC MAMMALIAN CELLS THAT SURVIVE IONISING RADIATION

C. B. Seymour, Carmel Mothersill and *Tikvah Alper

Saint Luke's Hospital, Rathgar, Dublin 6, Ireland and
**Birkholt, Sarisbury Green, Hampshire SO3 6AL*

Heritable changes induced by radiation in somatic mammalian cells may be expressed only after many normal divisions; it has been found that some of these changes may be lethal This was deduced from observations of reduced plating efficiency (PE) in distant descendants of irradiated cells, sometimes after more than 20 generations. Reductions in PE were dose-related and comparable for two very dissimilar cell lines: a primary culture from adult thyroid tissue and an "immortal" laboratory line (CHO-K1).

It is customary for mutation/transformation yields to be given "per surviving cell" These stated yields may be significantly underestimated if some survivors, as judged by conventional colony counts, have failed to give rise to viable progeny by the time the yields are scored. If, as seems likely, lethal mutations also occur in somatic cells irradiated *in vivo*, this would account for the fact, well known to radiotherapists, that tissue showing no overt sign of previous irradiation can stand very little further irradiation or exposure to cytotoxic drugs

THE EFFECTS OF LOCALISED PELVIC IRRADIATION IN THE RAT: THE INFLUENCE OF FIELD POSITIONING

G. A. Ross and J. W. Hopewell

CRC Normal Tissue Radiobiology Research Group, Research Institute (University of Oxford), Churchill Hospital,
Oxford OX3 7LJ

The pelvic large bowel of young adult rats was locally irradiated with a single dose of 23 Gy of X rays In one series, 30 mm of rectum, including the anal margin, was irradiated. In the other, the field was 20 mm long, based on the distal edge of the vagina, 10 mm proximal to the anal margin In both series, animals showed an early diarrhoea and a haemorrhagic proctitis. With the larger field size these reactions were transient; however, with the smaller irradiation volume, they often persisted until death. By 14 days after irradiation a $\geqslant 50\%$ contraction of the irradiated portion of rectum was noted at post-mortem examination.

In the first series of experiments, almost total denudation of the mucosa occurred within 7 days of irradiation This was closely followed by mucosal ulceration. Macrocolonies were present 2 weeks after irradiation and these increased in size with time; areas of ulceration become smaller but progressively deeper with time. An additional feature was the ingrowth of the epidermis from around the anal margin into the rectum. This covered areas of both ulceration and regenerating colonies No animal lethalities were observed for periods of > 16 months after irradiation. This was attributed to these epidermal ingrowths.

When the smaller field was irradiated, epidermal migration was prevented and mortalities occurred In a group of 17 rats, 59% were dead within 100 days after irradiation Rectal obstruction was seen in only 20% of these animals, whereas urinary-tract lesions accounted for 40% of animal deaths. Animals presenting with lesions commonly referred to as "late complications" always showed signs of a persisting acute mucosal reaction. This may have contributed to the observed damage and, therefore, these may not be true "late effects".

THE EFFECT OF FRACTIONED IRRADIATION ON THE RAT HEART

K. R. Trott and *S. Lauk

*Department of Radiation Biology, Medical College of St Bartholomew's Hospital, London EC1M 6BQ and *Institute of Radiobiology, GSF, D-8042 Neuherberg, Federal Republic of Germany*

After the localised irradiation of the heart, Wistar rats may develop fatal cardiac failure. With increasing dose, the latency decreased to reach a plateau at about 15 weeks after doses of $\geqslant 30$ Gy. Even doses as low as 17.5 Gy produced cardiac failure in all the irradiated animals after a latency period of 12–18 months. Fractionated irradiation was given in three, five, or 10 equal fractions, each after individual beam shaping Doses per fraction ranged from 5.5 Gy to 12 Gy In all schedules the overall treatment time was 4 weeks. The dose–response curves for the mean latency time to cardiac failure were well defined for single doses and after three fractions but showed considerable scatter for the five- and 10-fraction schedules Taking 42 weeks' mean latency as an isoeffect, an α/β value of 1 Gy was calculated.

THE RESPONSE OF THE MOUSE KIDNEY TO VERY LOW X-RAY DOSES PER FRACTION

M. C. Joiner, J. Denekamp and B. D. Michael

Gray Laboratory of the Cancer Research Campaign,
Northwood, Middlesex HA6 2RU

The effect of repeated exposure of the mouse kidney to very low doses of X rays has been studied using a "top-up" design of experiment Graded doses of neutrons ($\bar{E}_N = 3$ MeV) were used to bring subthreshold X-ray damage into the measurable range and hence obtain dose–response curves Kidney damage after bilateral irradiation with 30 X-ray fractions of 0.2–1.6 Gy was assessed by changes in ^{51}Cr-EDTA clearance, urine output and haematocrit at 16–50 weeks after irradiation. The best resolution was obtained at 29 weeks, with all three end-points.

These data were used to test the linear-quadratic formula as a description of the underlying dose–response curve. The model fits well down to doses per fraction of 1 Gy, below this dose there is an unexpected increase in the effectiveness of the X rays, which can also be seen as a decrease in the relative biological effectiveness (RBE) of 3 MeV neutrons relative to X rays at low doses The response to neutrons was effectively linear, but the RBE decreased from 10.6 to 6.6 when the dose per fraction was reduced below 1 Gy to 0.2 Gy It is postulated that this was due to the dominant influence of a sensitive population of cells at very low doses Modelling suggested that *all* cells were initially in a radiosensitive state, but that cells acquire increasing radioresistance when given repeated doses above 0.26 Gy This transfer to a more resistant response is complete at 1 Gy per fraction. A cell kinetic explanation has been proposed previously. An alternative hypothesis is that low radiation doses trigger or stimulate a repair system and this reaches maximum effect at 1 Gy

CHANGES IN DUODENAL ENDOCRINE CELL POPULATION AND VILLOUS STRUCTURE AFTER X IRRADIATION

M. G. Wyatt, *S. P. Hume, †K. E. Carr and *J. Marigold

Department of Surgery, Bristol University, Bristol BS2 8HW
**MRC Cyclotron Unit, Hammersmith Hospital, London*
N12 0HS and †Anatomy Department, Queen's University, Belfast

Gastrointestinal hormones have a well defined digestive role in the gastrointestinal tract. Although they are now known to have another equally important role as regulators of growth, their relative importance in the maintenance of epithelial structure remains unclear. Damage to the gastrointestinal endocrine cell population may directly influence subsequent crypt morphology and villous topography The aim of this study was to correlate changes occurring within the enteroendocrine cell population with subsequent alterations in epithelial structure.

Using a combination of light and scanning electron microscopic techniques, both cryptal and villous epithelial characteristics have now been studied and compared with values for endocrine cells/crypt Experiments were organised using both irradiated and unirradiated groups of mice. For the irradiated groups, two time points and three radiation doses (6, 10 and 18 Gy) were used Results indicated a significant drop in endocrine cell number at both 1 and 3 days after all three radiation doses. At low doses, endocrine cell recovery occurred between 1 and 3 days, whereas at medium and high doses, a further decline was noted. A similar pattern was observed when considering qualitative epithelial surface changes induced by X irradiation At medium and high doses, severe epithelial disruption was seen within both the cryptal and villous compartments. At low doses, however, crypt counts remained constant and epithelial surface damage was minimal.

It was concluded that both villous structure and crypt morphology were closely related to changes occurring within the cryptal endocrine cell population The exact nature of this relationship remains unclear and further work is required to determine the precise role of the gastrointestinal endocrine cells in the maintenance of normal epithelial structure.

INFLUENCE OF CIRCADIAN RHYTHMS ON RADIOSENSITIVITY IN MOUSE SKIN

B. Stadler, A. Rojas, J. Soranson and J. Denekamp

Gray Laboratory of the Cancer Research Campaign, Mount Vernon Hospital, Northwood, Middlesex HA6 2RN

It is well known that circadian rhythms occur in the cell proliferation parameters of several epithelial tissues In humans, this has been shown to influence their sensitivity to cycle-specific chemotherapeutic drugs. From work *in vitro* it would appear that the influence of cell cycle distribution on the response to X rays is larger at small doses A study of the influence of circadian radiosensitivity was undertaken using: five fractions of 1 Gy of X rays in 5 days followed by a variable neutron top-up dose, five equal fractions of X rays only (6.5–10 5 Gy/fraction), and large single doses (18–30 Gy). Groups of animals were irradiated at 1, 3, 5, 6, 7 a.m and 5 p.m. At the same times mice were also injected with tritiated-thymidine to determine the labelling and mitotic indices. For animals irradiated at 5 and 6 a.m. with five fractions of X rays alone, a small increase in sensitivity (enhancement ratio ~ 1 06) was found. No variation in radiosensitivity was observed in the rest of the experimental groups, suggesting no significant influence of circadian rhythm on the radiosensitivity of mouse skin.

The clinical use of electrons

Abstracts of papers presented at the above meeting, held at 36 Portland Place, London W1N 3DG, on Wednesday, February 26, 1986

Session I

Chairman: Dr W. F. White

The code of practice for electron beam dosimetry, by G. Pitchford
Physical basis of electron therapy, by S C Klevenhagen
Electron beam therapy in the treatment of mycosis fungoides, by M F. Spittle

THE CODE OF PRACTICE FOR ELECTRON BEAM DOSIMETRY

G. Pitchford

Cookridge Hospital, Leeds

The code of practice (Hospital Physicists' Association (HPA), 1985) for electron beam dosimetry in radiotherapy deals with: the calibration of an electron chamber against a second standard chamber in a photon beam, the use of this chamber to measure depth–ionisation curves in a suitable phantom, and the calculation of the absorbed dose to water from these measurements. The code recommends the use of a conversion factor, C_e, to obtain an absorbed dose to water using an electron chamber having an air kerma calibration factor N_f. The conversion factor has been given a new symbol C_e (compared with the old symbol C_E) following the change from an exposure to an air kerma calibration and the introduction of SI units The absorbed dose in water, D_w, is related to C_e by

$$D_w = R_e N_f C_e$$

where R_e is the corrected chamber reading and $N_f = N_s k_s$, where N_s is the calibration factor of the secondary standard chamber when irradiated in air using cobalt 60 and k_s converts this to an in-phantom calibration

The HPA code specifies the use of two designated ionisation chambers for which it provides C_e factors for measurements in water, polystyrene or perspex. Other, non-designated chambers can be used as field instruments provided they have been compared with one of the two designated chambers. A comparison of absorbed dose factors obtained from other recent protocols and the previous HPA code of practice is presented with reasons given for differences in these factors between the various protocols. An indication of the change in absorbed dose due to the implementation of the new HPA code is given. The use of polystyrene or perspex as phantom materials for the measurement of absorbed dose at a point on depth–ionisation curves is discussed with regard to two problems: ratio of ionisation readings in water and plastic due to electron fluence differences in the media, and charge storage following irradiation in insulating plastics.

REFERENCE

HPA, 1985. Code of practice for electron beam dosimetry in radiotherapy. *Physics in Medicine and Biology, 30,* 1169–1194

PHYSICAL BASIS OF ELECTRON THERAPY

S C. Klevenhagen

Department of Medical Physics, The London Hospital, London E1

The clinical application of fast electrons in radiotherapy started soon after the first electron accelerators were developed (Skaggs et al, 1948). However, only during the last 15 years, when the linear accelerators became widely available, has the electron's application developed to become an important radiotherapy modality (Karzmark & Pering, 1973; Greene, 1986). The features of the electron beam that make it attractive in radiotherapy are related to the beam's physical characteristics rather than to any special radiobiological effectiveness of electrons (Klevenhagen, 1985). It is therefore essential to know and understand the physical behaviour of electrons during their transition through tissue in order to be able to utilise properly the electron beam to its full capacity.

The physical phenomena associated with electrons are quite different from those associated with photons. Electrons are characterised by negative charge and small mass, which make them susceptible to frequent collisions. These interactions lead to fast energy losses resulting in limited range of the beam in tissue and to lateral spread of the beam caused by scattering. These processes provide an explanation for the characteristic features observed in both the central axis and the two-dimensional electron beam distributions such as the small absorbed-dose build-up, the peak of the distribution curve and the fast fall-off of the dose with depth. The latter feature is the most important advantage of electrons since it contributes to the sparing of tissue beyond the boundary of the tumour volume.

In clinical application, the therapeutic range of an electron beam is varied by selecting the appropriate beam energy. At higher energies, when a treatment of deeper-sited tumours is attempted, the presence of inhomogeneities needs to be considered. Inhomogeneities affect the beam absorption and scattering, producing considerable changes in the beam distribution. Corrections for inhomogeneities as well as for body surface irregularities are best performed in suitably designed computerised treatment planning systems which employ computed tomography data. There are at present very few electron beam computational models. Among them the age-diffusion, based on the pencil beam model, and multiple-coulomb-scattering models are the best.

REFERENCES

GREENE, D., 1986. *Linear Accelerators for Radiation Therapy.* (Adam Hilger, Bristol).

KARZMARK, C J & PERING, N. C., 1973 Electron linear accelerators for radiation therapy. *Physics in Medicine and Biology, 18,* 321–354

KLEVENHAGEN, S C, 1985. *Physics of Electron Beam Therapy.* (Adam Hilger, Bristol).

SKAGGS, L S., ALMY, G. M., KERST, D W. & LANZL, L. H., 1948. Development of the betatron for electron therapy. *Radiology, 50,* 167–172

ELECTRON BEAM THERAPY IN THE TREATMENT OF MYCOSIS FUNGOIDES

M. F. Spittle

The Middlesex Hospital, London

Whole-skin electron beam therapy is an important aspect of the treatment of mycosis fungoides. It was pioneered by Drs Szur and Bewley at the Hammersmith Hospital. Mycosis fungoides is a rare skin lymphoma, the manifestations remaining entirely dermatological usually for much of the natural history of the disease, which may last up to 40 years. The disease was described by Alibert and, in addition to the classical form of the disease, other variants are the erythrodermic form, poikiloderma atrophicans vasculare, and the Worringer-Kolopp variant. The Sezary syndrome is the leukaemic phase of this cutaneous T-cell lymphoma, although the clinical aspects of the Sezary syndrome are dissimilar to mycosis fungoides.

Differing forms of therapy are appropriate at the various stages of mycosis fungoides. For an initial protracted period the superficial eczematous-like process can be controlled with topical steroids, emollients or ultraviolet light. When the disease becomes more infiltrated, appropriate therapy should be instigated. In some centres considerable reliance is placed on the efficacy of topical nitrogen mustard treatment. This entails diluting mustine in water and spreading the solution over the skin daily or several times a week. This is a time-consuming and expensive procedure and results in a high incidence of sensitisation. Mustine can now be produced in an emulsifying ointment which is easier to apply. In Great Britain the treatment of intermediate-stage mycosis fungoides by Psoralen-ultraviolet-A (PUVA) therapy has been investigated. Psoralen is used as a sensitiser to UVA and the patient receives treatment initially two or three times a week. This therapy may be maintained on a weekly or fortnightly basis, during which time the skin becomes pigmented. For those patients for whom topical nitrogen mustard or PUVA therapy is not sufficient to prevent the disease becoming more infiltrated and for those who present with widespread tumour-stage mycosis fungoides, electron beam therapy is the treatment of choice. The 4 MeV beam is decelerated by carbon and passes through a gold scatterer, producing a beam which at 6 m is able to treat the whole of a standing patient. The patient is off-centred to the main axis of the beam to minimise X-ray contamination. The patient is treated with an eight-field technique twice weekly, four fields being treated each day. The skin receives approximately 300 cGy twice weekly from the accumulated dose from the eight fields. The treatment is continued for 5 weeks, giving a total of 3000 cGy. The patient's head may be shielded by a perspex plate if it is not affected by disease and this will prevent temporary epilation which may follow treatment. The eyes are shielded and the fingernails, if not shielded, will be shed. The 80% depth dose of the beam reaches approximately 1 cm, which is appropriate for most clinical situations. Patients with more aggressive tumours and with disease in areas not treated by this eight-field technique have further top-up doses with low-energy X rays. This is a most successful treatment. No systemic symptoms are noted and there is no haematological abnormality following electron beam therapy. Almost all patients have their disease cleared by the treatment and maintenance therapy with PUVA or topical nitrogen mustard is helping to continue these remissions. The particular importance of electron beam treatment in mycosis fungoides is that, although a T-cell lymphoma, the disease is, in general, resistant to chemotherapy. Although the number of patients with mycosis fungoides is small, it is important that some centres have apparatus dedicated to this treatment.

Session II

Chairman: Dr W. F. White

An overview of high-energy electron equipment, by K. Larkin
Quality assurance for electron beam therapy, by P. C. Williams
Some clinical uses of electron beam therapy, by T. G. Landberg

AN OVERVIEW OF HIGH-ENERGY ELECTRON EQUIPMENT

K. Larkin

M.E.L., Radiotherapy Division, Manor Royal, Crawley, West Sussex RH10 2PZ

The limited use of electron fields may be related to difficulties in both treatment planning and treatment delivery. Various beam collimation systems are discussed to see how each of these compare with a number of idealised requirements. Of those systems considered, the optimal scatter system would appear to meet the majority of the requirements and offer the flexibility for future dose-distribution modelling to specific target volumes

QUALITY ASSURANCE FOR ELECTRON BEAM THERAPY

P. C. Williams

Christie Hospital, Manchester

Quality assurance for electron beam therapy is not a new subject but is, and has been, essential in the development of safe and effective radiotherapy. It is a process which starts before a machine is ordered and which should continue throughout its clinically useful life. The first part of quality assurance is to focus the specification of equipment on those areas which are clinically significant. The second involves detailed performance testing during commissioning, followed by a regular programme of performance tests to ensure that the equipment is maintained within specification. These tests must be carried out at frequent intervals for each of the electron energies used. It is therefore essential that tests are both sensitive and simple. Simple tests for stability of dose delivery, field flatness, beam energy, field size and X-ray contamination are described. Finally physicists, who are the group identified to be best suited to carry out the quality assurance programme, have to be continuously aware of how the equipment is being used, so that all treatments can be carried out within the limitations of the equipment and the physical principles of electron beam therapy, and so that the testing of the equipment, which is seen as a feedback mechanism, can be appropriate to the treatments being carried out.

SOME CLINICAL USES OF ELECTRON BEAM THERAPY

T. G. Landberg

Department of Radiotherapy and Oncology, University Hospital, S-214 01 Malmö, Sweden

Experience, up to now, with electron beams of energies ranging from 4 to 45 MeV, being produced by betatrons, linacs, or microtrons, has shown that electron therapy may be useful in certain clinical situations Low energies (4–7 MeV) have been used in the therapy of skin tumours and the chest wall after mastectomy. Electrons of somewhat higher energies (10–12 MeV) may be considered in the therapy of lip cancers, superficial recurrences, and as a boost in breast cancers For the treatment of internal mammary nodes, at least 14 MeV electrons are needed. Energies in the range 20–25 MeV may be useful in many ear, nose and throat tumours, *e.g.* carcinoma of the parotid gland. Higher energies (25–45 MeV) have so far been used very little, but may be considered in some pelvic tumours Improvements are needed, including better and larger electron beams (dual scattering foils, thin ionisation chambers, scanning beam electrons), more flexible collimating systems (multileaf collimators), and better dose planning systems (based on, for example, pencil beam algorithms). With such improvements, electron beam therapy may well be even more useful.

Book review

Clinical Diagnostic Ultrasound Ed. by Ellis Barnett and Pat Morley, pp. 616, 1985 (Blackwell Scientific Publications, Oxford), £120.
IBN 0–632–00897–0

This book should have been a classic. Edited by two of the most eminent sonographers in the United Kingdom, it draws on the expertise of some of the foremost workers in ultrasound in the UK and Australia. The book was to cover the whole gamut of ultrasound imaging in a single volume. The text is informative as well as being readable and concise. It is therefore dismaying and depressing that a book of such magnitude and authority should appear so hopelessly out of date. While it is accepted that, particularly with a multi-author text, there will be delay in publication, it appears that the delay in this case has been a full 5 or 6 years. The most recent references in some of the sections are to articles written in 1977. Some of the authors have clearly made a valiant attempt to bring their texts and references up to date, but these attempts are made obvious by the haphazard nature of some of the references. Other sections are clearly more current, indicating either that they have been completely revised during the preparation of the book or that they were submitted later, thus contributing to the delay in its appearance.

Images throughout the book, although well reproduced, do not demonstrate current equipment capabilities and most are derived from static compound B-scanners. While the use of a static compound B-scanner should not in itself be criticised when a large field of view is needed, the images reflect the age of the text since real-time scanners are described as new and unlikely to replace static B-scanners in the production of detailed diagnostic images.

The text contains much to recommend it. Although the introduction of real-time scanning has modified techniques, optimal scan planes have changed but little. The careful description of salient points of anatomy together with a consideration of tissue pathology and the effect this has on the ultrasound images represents, in my view, the proper approach to diagnosis by ultrasound. Similarly, consideration of other methods of image production, as exemplified by the section on the thyroid, demonstrates clearly the interaction of ultrasound with other diagnostic radiological procedures.

Finally, however, I am left with the feeling that I wish I were reviewing this book in 1981, in which case by now I should be eagerly awaiting a new edition, but I wonder whether the authors or indeed the editors will have the heart to embark upon a new edition after the frustration that this one must have caused. This book must have been at least 7 or 8 years in the making and that, sadly, in ultrasound is too long a gestation.

P A DUBBINS

BIR Welsh Branch: 1986 Spring Meeting

The Spring Meeting of the Welsh Branch of the BIR was held at Prince Charles Hospital, Merthyr, on Saturday, June 4, 1986. Dr John Parker was the organiser and chairman of the meeting and the theme of the symposium was urinary infection in children. Abstracts of the lectures are given below.

The 1986 Autumn Meeting of the Welsh Branch will be held at the University Hospital of Wales, Cardiff, on Saturday, November 8, 1986.

Medical aspects

Kate Verrier Jones, Paediatric Nephrologist, Cardiff

Bacterial infection of the urinary tract is one of the commonest childhood infections. Urinary-tract infections often start in the first year of life, when there is also the greatest risk of developing renal scarring, particularly if vesico-ureteric reflux is present. In infants, symptoms are not related to the urinary tract and the collection of urine samples is difficult, so that the diagnosis is easily missed. Early treatment may reduce the risk of renal damage. Subsequent investigation of the urinary tract is primarily to exclude obstruction, which occurs in 5% of children with proved infection. It is also helpful to document the presence of renal scarring, which is associated with a reduction in glomerular filtration rate and an increased risk of hypertension. The presence of vesico-ureteric reflux will influence the management of the younger child, but the best way to manage children with this condition is still under investigation. With reliable renal ultrasound, the need for intravenous pyelography is reduced. Doubts about the benefit of ureteric reimplantation have reduced the need to undertake micturating cystography, an investigation which is often upsetting for the child and then difficult to undertake.

Surgical aspects

J Lari, Paediatric Surgeon, Cardiff

In a child with urinary infection, it is important to show the clinician whether there are any abnormalities in the urinary tract that require surgical intervention or careful follow-up. At the same time, overinvestigation should be avoided. The clinical findings play an important part in determining the timing and the order of various radiological investigations. It is important to exclude obstruction in the urinary tract at an early stage, as this needs early surgical intervention.

In children over the age of 5 years with urinary infection there is little risk of scarring of the kidneys. The first line of investigation is usually a radiograph of the abdomen to exclude renal calculi, followed by an ultrasound scan of the urinary tract. If this is normal, the child is followed up, otherwise an intravenous urogram is performed and, if necessary, other investigations such as micturating cysto-urethrography or radionuclide renography. In children under 5 years, a plain abdominal radiograph and an ultrasound scan may be followed by an intravenous urogram (IVU) or a micturating cysto-urethrogram or both, depending on the findings. Radionuclide studies are performed if necessary. If obstruction is suspected, then a DTPA scan with Lasix (Hoechst UK Ltd) not only confirms obstruction but gives a differential function of the kidneys. In the case of vesico-ureteric reflux, a DMSA scan is performed to look at the cortical map, the renal tubular-cell mass, as well as the differential function of the kidneys. In very young infants (under 3 months), the radionuclide studies are often performed before the IVU, as the kidneys do not always sufficiently concentrate the contrast medium.

The young infant presenting with urinary infection often has a complicated congenital anomaly. It is important in these cases to discuss the patient with one's radiological colleague to decide how best to proceed with the radiological investigation.

Radiological investigations

T. Sherwood, Professor of Radiology, Cambridge

A urinary infection is a common event in childhood. There is a natural desire by parents and doctors that a normal urinary tract without vesico-ureteric reflux should then be documented with complete certainty. Even in an ideal world this would be much resented by the patients, since a routine cystogram would be required. The pay-off from such strategies is poor, and the scope for effective medical intervention limited. Stones and drainage anomalies are the important and correctable abnormalities that must be found, and various diagnostic tactics were discussed for different age groups.

Ultrasound investigations

Tina Hayward, Senior Lecturer in Radiology, Cardiff

Ultrasound plays an important role in the initial investigation of urinary-tract infection in childhood. A high-frequency real-time sector scanner is used. Sedation is never necessary, although adequate time spent explaining the investigation to older children is beneficial. The only preparation necessary is to ensure the bladder is full whenever feasible.

The normal renal appearances were considered in terms of central sinus echoes, cortical echogenicity and medullary pyramid echogenicity and the varying features throughout childhood were demonstrated. The pitfalls encountered were also discussed. The abnormalities expected were classified, reflux and obstruction being the most common underlying causes of infection, and illustrative examples were shown. The importance of recognising renal anomalies was stressed. The paper concluded with a recent review of the ultrasound findings in 60 children presenting with urinary-tract infection. The 16 abnormalities encountered were described and discussed. It was emphasised that scans of the highest quality should be obtained and if considered abnormal, equivocal or inadequate, further radiological assessment is necessary.

Radionuclide studies

Helen Carty, Paediatric Radiologist, Liverpool

The two main radionuclide investigations in urinary-tract infection are renal imaging with $^{99}Tc^m$ dimercaptosiccinic acid (DMSA) and radionuclide cystography. The problems of when to use radionuclide investigations and why and where they should be used were addressed. It was suggested that where facilities were not available on site, it was comparatively easy to arrange a session for paediatric patients which would improve the facility and acceptability of studies, both for nuclear medicine staff and for paediatricians. Technical aspects of scanning children were briefly discussed. The varying appearances of renal damage due to reflux and some of the pitfalls in interpretation were described. The indications for DMSA scanning are: known abnormality on intravenous urography or known reflux, breakthrough infection, pre-operatively, renal ectopia, follow-up, and baseline and follow-up assessment of children with neuropathic renal disease.

The technique of radionuclide cystography by both direct and indirect methods was described. It is still not acceptable as the primary investigation in small children in Britain due to the poor anatomical detail, but it is now the first choice in older children and in all repeat cystography. Its sensitivity is much greater and the radiation dose much less than those in conventional micturating cysto-urethrography.

The new President

Professor Roger Berry, the Institute's new President, was born in New York, where he did his first degree, in physics and biology, at New York University and entered the radiological world as a very junior physicist in New York's Hospital for Joint Diseases where, under the direction of the late Dr Milton Friedman, the first 2 MV air resonance transformer X-ray generator for clinical radiotherapy was installed. He moved to Duke University, Durham, North Carolina, for medical training, qualifying in 1958. He came to Oxford to work with Dr Frank Ellis, but was recalled for US military service, spending 2 years at the National Institutes of Health, Bethesda, where his major contributions were the development of *in-vivo* mammalian systems for measuring survival of tumour cell reproductive capacity and the application of these to understanding biological effects of fast neutrons and charged particles, as well as understanding such phenomena as effects of radiation dose-rate and dose fractionation. He also made contributions to understanding interactions of radiation and the effects of cytotoxic drugs.

Having returned to Oxford in 1962 to succeed Dr Laszlo Lajtha as Head of the Radiobiology Laboratory at the Churchill Hospital, and having completed his D.Phil at Magdalen College, he became a British national and joined the Royal Naval Reserve. There his career took him unexpectedly to extended service in nuclear submarines.

Professor R. J. Berry

He was recently promoted Surgeon Captain and will shortly become the Principal Medical Officer (Reserves). He moved from Oxford to the Medical Research Council Radiobiology Unit, Harwell, as Head of Neutrons and Therapy-Related Effects Laboratory and then to the Middlesex Hospital as Professor of Oncology in 1976. As he was, at the time, pursuing laboratory science, he was the non-medical Secretary of the Institute from 1970 to 1973, but he will now be a medical President. He has just completed his year as President of the Radiology Section of the Royal Society of Medicine.

He was elected a Commissioner of the International Commission on Radiological Protection in 1985 and is a member of the National Radiological Protection Board, the MRC Committee on the Effects of Ionising Radiation (and Chairman of its Radiobiology Sub-Committee), the DHSS Committee on the Medical Aspects of Radiation in the Environment, and the Department of the Environment's Radioactive Waste Management Advisory Committee, having served on Sir Douglas Black's enquiry on Sellafield. He is at present Vice-Chairman of the British Committee on Radiation Units and Measurements and is Chairman of the Scientific Advisory Committee of the Thames Cancer Registry, which was created in 1985 to serve the four Thames regions.

He married his wife, Valerie, a radiographer, in 1960. His hobbies include an unquenchable passion for sailing, jazz music, and an enthusiasm for the Institute which has taken him through the secretaryship and/or chairmanship of several of its committees and over 13 years on its Council.

Obituary

Curt Westman

Curt Westman, Honorary Member and friend of the British Institute of Radiology, died in Stockholm in July at the age of 72.

Many British radiologists will remember Curt Westman with affection for his friendship, his cultured charm, his kindliness and his generosity, but none more so than those registrars who gained their first radiological experience overseas in his Stockholm clinic. For it was he who was personally responsible for the Westman scholarships awarded over the last 25 years by the Institute to enable young British radiologists to visit Sweden and to spend time not only working with him, but also observing and experiencing the stimulating atmosphere of Swedish radiology. The lasting professional value of these visits, together with memories of the personal warmth of the hospitality offered by both Dr and Mrs Westman, form the common thread of experience shared by those fortunate visitors over the years.

Curt Westman was born in Västerås and graduated from medical school in Stockholm in 1944. He trained in radiology, both in the Seraphimer Hospital, where he worked with Erik Lindgren and others, and at the Karolinska Institute between 1944 and 1955. In the late 1950s and early '60s he established, somewhat against the odds, the Vällingby Clinic, a private institution, unusual in Sweden. The concepts and design of this clinic enabled him to demonstrate his remarkable planning abilities and to produce a facility which has been a model of efficient and kindly radiological practice. The clinic, with its interdisciplinary links and its own subway station for easy access, enabled him to pursue his objectives of efficient patient care without compromise in technical standards.

Curt Westman was truly a man for all seasons—doctor, businessman, bon viveur, bibliophile and antiquary. He had a rare ability to extract the best things from life to share with others; a true life enhancer. An enthusiastic car driver, he travelled all over Europe in both large and small vehicles, liaising with industrial colleagues, exploring radiological possibilities and establishing new friendships wherever he went. He frequently visited Britain and was a regular attender of BIR meetings and the Annual Congresses. He took particular pleasure in the Honorary Membership of the Institute awarded in 1978. He was especially thrilled to take part in the official opening, by Her Majesty the Queen, of 36 Portland Place in 1982.

While retaining his interests in radiological practice, especially mammography, and in technological developments to the end, he was just beginning to enjoy semi-retirement when he developed his fatal illness. I had the personal privilege to be in Stockholm the week before he died and to visit him in hospital. He was looking forward to receiving another registrar this year and we reminisced with pleasure about lovely spring days in England.

To Barbara, his wife, and to his children, Lars and Eva, the Institute extends its deepest sympathy.

IAN ISHERWOOD

Pioneers and Early Years: a history of British radiology

This book, by E. H. Burrows, traces Röntgen's experiments in 1895 and the British reaction to his announcement of "the new sort of rays", subsequently called X or Röntgen rays. The first experimenters are named, including the doctors who pioneered the introduction of X rays into clinical use in Britain. Early apparatus makers, mostly optical instrument makers, and their machines are described and illustrated. The growth of radiology as a medical specialty up to 1930 is outlined, including the early societies, the Cambridge D.M.R.E. diploma and the establishment of the British Institute of Radiology. *The Archives of Clinical Skiagraphy* (1896) was the first radiological journal in the world, and the Röntgen Society (1897) was the first X-ray society; each continues to flourish to the present day as the *British Journal of Radiology* and the Institute. A separate section deals with the first military use of X rays in campaigns on the Nile, the North-West Frontier and South Africa. The final chapter records the mutilation and suffering of the early victims of X irradiation and the first counter-measures, and lists the British names on the Martyrs' Memorial in Hamburg. A feature of the book is the biographical sketches of the early pioneers, which add topicality and a personal interest to the story.

Published by Colophon Limited, pp. 264 + index, 1986, price £32.50. ISBN 0 95116760 x.

Press releases

Annual meeting of the RSNA

Radiologists from around the world are expected to attend the 72nd Scientific Assembly and Annual Meeting of the Radiological Society of North America (RSNA), scheduled for November 30–December 5, 1986, at McCormick Place in Chicago. This year's meeting will feature presentation of more than 1000 scientific papers covering nine radiological subspecialties and more than 319 scientific exhibits.

Honorary memberships will be presented to: Dr Hikoo Shirakabe, Professor of Internal Medicine, School of Medicine, Juntendo University, Tokyo, Japan; Dr Jacqueline Vignaud, Chief of Service, Radiology Department, Foundation de Opthalmologique A. de Rothschild, Paris, France; and to Dr Bjorn E. W. Nordenstrom, Professor of Radiology, Karolinska Institute, Stockholm, Sweden.

Among high points of the programme will be Dr McCort's presidential address, which will discuss the changing patterns of trauma care, and the Arthur W. Erskine Lecture by Dr Robert G. Parker, Los Angeles, who will speak on precision in the diagnosis and treatment of cancer

Other special sessions and courses will focus on spinal and breast imaging and radiation therapy treatment planning. An overview of key innovations in radiology during 1986 will be given by Dr Stanley S. Siegelman, Baltimore, editor of *Radiology*, the official journal of RSNA

A joint symposium of RSNA and the American Association of Physicists in Medicine will be devoted to progress in magnetic resonance spectroscopy Radiolabelled antibodies for diagnosis and treatment will be the subject of the Eugene P. Pendergrass New Horizons Lecture given by Dr Steven M. Larson, Bethesda

In view of the increasing use of nuclear energy, another special programme will be "Nuclear Reaction Accidents, Radiation Injury, and the Role of the Radiologist" to be conducted by Eric J Hall, Ph D, Department of Radiology, Radiological Research Laboratory, Columbia University, New York.

3M laser imager sets new standards

The new 3M Laser Imager is now fully available and establishing a new standard for quality and productivity in diagnostic imaging

Image quality far superior to that possible with cathode-ray tube type multiformat cameras is provided by the 3M Laser Imager. The use of an IR semiconductor laser diode totally eliminates problems such as phosphor noise, geometric distortion and monitor drifting, normally expected with conventional multiformat cameras. One, four, six or 12 images, containing up to 4000 × 5000 × 8 bit pixels, may be recorded on a single sheet of film 35 cm × 43 cm, thus allowing up to 256 grey levels for each pixel Each image can be placed in any position on the film, with negligible acquisition time to facilitate "quick" software packages Images can also be erased and relocated.

Black or clear borders between images are possible The user may prefer to select black borders to reduce glare and eye fatigue, at the same time increasing sensitivity to image detail

The 3M Laser Imager houses a digital, random access memory system Multiple originals can be produced very simply, by setting the automatic image counter Each original produced will be identical to the next. Loss of image quality and time-consuming routines, associated with conventional film storage and duplication, can therefore be eliminated Digital electronics are used to magnify images to the required sizes, thus avoiding the problems and improving the quality associated with conventional optics Both "smooth" (interpolation) and "sharp" (replication) image-display methods are available

Remote contol is a standard feature of the 3M Laser Imager. The operator keypad can be located up to 200 feet away from the imager. Control by sources such as computed tomography or magnetic resonance systems can be implemented through a standard RS232/422 serial interface

The imager magazines will hold up to 125 sheets of film, preventing the need for continual loading of individual cassettes The unit may also be linked directly to a film processor 3M Laser IR Film (patent applied for) has been specifically designed for use with the 3M Laser Imager. Its infra-red sensitive, silver-halide emulsion is totally compatible with the infra-red emission of the laser and has been specially developed by 3M to eliminate interference patterns caused by reflected light Unlike other infra-red sensitive films, 3M Laser IR Film does not require special refrigerated storage conditions.

3M has worked very closely with major equipment manufacturers on interface requirements The 3M Laser Imager can be supplied via an imaging system manufacturer as part of an installation specification or directly from 3M United Kingdom PLC The 3M Laser Imager has been designed to accommodate future advances in image receptor systems. The unit is easy to upgrade, with memory expansion possible by simple addition of memory boards Analogue links are available where needed and the 3M Laser Imager may also be retrofitted to existing installations to improve image quality 3M technological developments will facilitate multimodality input to one laser imager.

Further details. 3M United Kingdom PLC, 3M House, PO Box 1, Bracknell, Berkshire RG12 1JU (Tel. 0344-426 726)

Multiple-frequency hand-held Doppler scanner

The Pocket-Dop II™, manufactured by Imex Medical Systems is the first hand-held Doppler scanner to offer the convenience and versatility of interchangeable probes. One small instrument can be used in over 40 vascular and obstetric applications. Choose the 5 MHz or 8 MHz probe to screen for peripheral vascular disease such as arteriosclerosis, venous thrombosis and cerebral vascular insufficiency Switch to a 2 MHz or 3 MHz obstetric probe to determine fetal well being and reassure the expectant mother

The Pocket-Dop II™ features a built-in speaker with insertable earphones for private monitoring, an improved, longer cord for easier use, a convenient rechargeable 110 or 220 V battery and a sturdy carrying case with an improved latch for added safety. Probes are now labelled for quicker identification The 5-year parts warranty is unmatched in the industry, and a new service warranty is available after the manufacturer's warranty lapses. For more information contact Imex Medical Systems, Inc, 6355 Joyce Dr., Golden, CO 80403, USA (Tel. toll-free 800-525 2519).

Magnetic resonance imaging health and safety

The magnetic and radio-frequency (RF) fields associated with magnetic resonance imaging (MRI) are a source of unique and largely unexplored health and safety concerns. Recently, the growing popularity of this new medical diagnostic tool has led more and more researchers to take a close look at its potential health effects and prompted health officials in the US, as well as abroad, to establish safety guidelines for its use

A special report by the editors of *Microwave News*, a newsletter based in New York, on the effects of non-ionising radiation exhaustively surveys the latest research findings from this growing body of literature This new publication, *NMR Imaging Health and Safety: an annotated bibliography*, by Louis Slesin, Ph.D. and Amy Rosenberg, M P.H., provides individual summaries of more than 50 citations from major scientific journals, books, trade publications and conference papers. It covers general reviews of health and safety issues, recommended guidelines for patient and operator exposures, biological effects of the magnetic and RF fields, cardiac pacemaker interference, implant and other ferromagnetic hazards, and site planning for NMR imager installations.

The report is available for $18.95 from *Microwave News*, PO Box 1799, Grand Central Station, New York, NY 10163. Only pre-paid orders will be accepted

Library news

The BIR Library is open weekdays 9 a.m.–5 p.m. (7 p.m. on Thursdays)

The Librarian, Mrs Gunnel Ingham, is in attendance Tuesdays 11 a.m.–5 p.m., and Thursdays 11 a.m.–7 p.m., and Mrs Angela Lansdown, daily 9 a.m.–5 p.m. (Tel. 01-580 4085).

The journal stock includes more than 100 titles. Though journals may not be taken out of the library, there is a photocopy service, also available by post. A list of current journals is available on request and is also published in the March and September issues of the Bulletin.

Most books (excepting the historical collection) are available on loan.

Recent additions to the Library

Ansell, G.: Radiology of adverse reactions to drugs and toxic hazards. 1985

Baert, A. L., et al (Eds): Frontiers in European radiology. Vol. 3. 1984

Fischer, A. Q., et al: Paediatric neurosonography: clinical, tomographic and neuropathological correlates. 1985

Holman, B. L.: Radionuclide imaging of the brain. 1985

Hope-Stone, H. F. (Ed.): Radiotherapy in clinical practice. 1986

ISRRT: Quality control handbook. 1986

NCI Monograph No. 70: Forty-five years of cancer incidence in Connecticut: 1935–79. 1986

NCRP Report 58: A handbook of radioactivity measurements and procedures. 2nd edit. 1985

NCRP Report 80: Induction of thyroid cancer by ionizing radiation. 1985

Sharp, P.F.; Dendy, P. P. & Keyes, W. I.: Radionuclide imaging techniques. 1985

Sovak, M. (Ed.): Radiocontrast agents. Handbook of experimental pharmacology. 73. 1984

Stockley, S. M.: A manual of radiographic equipment. 1986

Thakur, M. L. (Ed.): Radiolabeled cellular blood elements. Pathophysiology, techniques and scintigraphic applications. 1985

WHO (Scientific Group): Future use of new imaging technologies in developing countries. 1985

Advance Notice

British Institute of Radiology 45th Annual Congress, incorporating the joint BIR/RCR/RSM (Section of Radiology) spring meeting

RADIOLOGY '87

University of Southampton
April 1–3, 1987

The Congress will cover all aspects of radiology—X-ray diagnosis, radiotherapy, radiation oncology, nuclear medicine, ultrasound, NMR, radiological physics, radiobiology, radiation protection and related disciplines and is expected to include:

The BIR Mackenzie Davidson Memorial Lecture, by Professor M. J. Peckham, "The clinical biology of testicular germ cell tumours"

The BIR Mayneord Lecture (sponsored by 3M UK plc), by Dr Frances Fry, "Chernobyl reactor accident—the impact on the United Kingdom"

The RCR George Simon Lecture, by Dr J. C. Batten, "Radiology and cystic fibrosis"

The BIR Presidential Address, by Professor R. J. Berry, "The Institute at 90—a time for reappraisal?"

The BIR Annual Dinner will be held at the Polygon Hotel, Southampton, on April 2.

Proffered papers and posters are invited. Please apply to BIR for form. Absolute closing date for receipt of completed proffered paper forms is November 30, 1986.

For further information please apply to the Assistant Secretary: Programme, The British Institute of Radiology, 36 Portland Place, London W1N 4AT (Tel. 01-580 4085).

BIR calendar events

Unless otherwise indicated, enquiries about the following events should be addressed to the Assistant Secretary: Programme, British Institute of Radiology, 36 Portland Place, London W1N 4AT (Tel. 01-580 4085).

The meetings are at 36 Portland Place unless otherwise stated. Attendance is open to non-members.

Diagnostic and Therapeutic Uses of Radioisotopes in Oncology

November 26, 1986 at 10.30 a.m.
All day meeting organised by Nuclear Medicine Subcommittee.
Chairmen: Professor R. J. Berry and Dr R. T. D. Oliver.

Practical Aspects of Magnetic Resonance Imaging

January 14, 1987 at 9.30 a.m.
Middlesex Hospital Medical School, London
Chairman: Professor I. Isherwood. Speakers: Dr M. Smith, Dr G. Bydder, Dr B. Kendall, Professor I. Isherwood, Dr J. P. R. Jenkins, Professor B. Worthington and Professor J. J. K. Best.
Joint BIR/RCR meeting.

Uroradiology Update

January 15, 1987 at 5.30 p.m.
Chairman: Dr D. Rickards. Speakers: Dr D. Rickards, Dr J. Pemberton, Dr C. E. L. Freer, Mr G. Watson, Dr R. Johnson, Dr W. Lees, Professor D. J. Allison.
Joint BIR/RCR/RSM meeting.

Radionuclide Investigations of the Lung

February 11, 1987
Joint IPSM/BIR (Nuclear Medicine Subcommittee) all day meeting organised by IPSM.

All day non-topic proffered papers meeting

February 13, 1987
Joint ARR/BIR (Radiobiology Subcommittee) meeting organised by the Association for Radiation Research.

Picture Archiving and Communications Systems

February 25, 1987
Venue to be announced
Chairman: Professor I. Isherwood. Topics will include image display, image transmission and image storage.
All day meeting organised by Industry Committee.

Annual General Meeting

May 14, 1987 at 4.30 p.m.

Imaging in Radiotherapy

May 15, 1987
Chairmen: Dr D. Thwaites and another to be announced.
Joint IPSM/BIR all day meeting organised by IPSM.

Dysphagia and Disorders of Swallowing

May 20, 1987
Royal Society of Medicine, London
Joint RSM/RCR/BIR all day meeting to be organised by the RSM.

Conversazione

May 20, 1987
Royal Naval College, Greenwich

Meetings and courses

As a service to our readers, the title, date and place of meetings and contact address will be inserted free of charge any additional information will be charged at £1 75 per printed line, per insertion. Please contact the Managing Editor

Asian Regional Conference of The International Organisation for Medical Physics
December 8–12, 1986
Bombay, India
Further details: Organising Secretary. Asian Regional Conference on Medical Physics 1986, Association of Medical Physicists of India Division of Radiological Protection, Bhaba Atomic Research Centre, Bombay 400 085, India

The British Medical Ultrasound Society 18th Annual Scientific Meeting
December 16–18, 1986
University of Warwick, Coventry
Further details: Mrs L Blench, General Secretary, BMUS, 36 Portland Place, London W1N 3DG (Tel 01-636 3714).

Chest Radiology
January 12–16, 1987
San Diego, California
Further details R Dawne Ryals, PO Box 920113, Norcross, GA 30092-0113, USA (Tel. 404-641 9773).

Annual Update on Nuclear Radiology
January 16–18, 1987
San Diego, California
Further details. R. Dawne Ryals, PO Box 920113, Norcross, GA 30092-0113, USA (Tel. 404-641 9773).

Reactor Accidents: what Chernobyl has taught us
January 28, 1987
City Conference Centre, London
Further details: Professor J. H Martin, Department of Medical Biophysics, Building 15, Park Wynd, University of Dundee, Dundee DD1 4HN.

2nd International Symposium on Magnetic Resonance Imaging: MR '87
January 29–February 1, 1987
Garmisch-Partenkirchen, West Germany
Further details: Sekretariat Professor Dr J. Lissner, Radiologische Klinik, Klinikum Grosshadern, Marchioninistr. 15, 8000 Munchen 70, West Germany (Tel 089-7095 2750).

6th Annual Winter Congress in Medical Diagnostic Imaging
January 31–February 7, 1987
Cortina D'Ampezzo, Italy, and
6th Annual Winter Seminar in Medical Diagnostic Imaging
February 7–11, 1987
London
Further details Winter Seminar, Medical Seminars International, 21915 Roscoe Boulevard, Suite 222, Canoga Park, CA 91304, USA (Tel 818-701 5143)

Radiology: Imaging and Intervention
February 2–6, 1987
San Diego, California
Further details R Dawne Ryals, PO Box 920113, Norcross, GA 30092-0113, USA (Tel. 404-641 9773)

Thoracic Imaging 1987
February 16–19, 1987
Orlando, Florida
Further details R Dawne Ryals, PO Box 920113, Norcross, GA 30092-0113, USA (Tel 404-641 9773).

Perspectives in Radioprotection
March 13–14, 1987
Bethesda, Maryland
Further details. Dr Joseph F. Weiss, Armed Forces Radiobiology Research Institute, Bethesda, MD 20814-5145, USA

The Finzi Lecture
April 15, 1987
Royal Society of Medicine, London
"The solitary pulmonary nodule" by Dr S. Segalmann.
Further details: Royal Society of Medicine, 1 Wimpole Street, London W1M 8AE.

VI Congress of the European Association of Radiology (ECR '87)
May 31–June 6, 1987
Lisbon, Portugal
Further details Secretariat ECR '87, SPRMN, Av. Elias Garcia, 123–7° DTo, 1000 Lisboa, Portugal, (Tel: 77–05 30, Telex 62074 SPRMN P)

34th Annual Meeting of the Society of Nuclear Medicine
June 2–5, 1987
Toronto, Canada
Further details: Society of Nuclear Medicine, Education & Meetings Department, 136 Madison Avenue, New York, NY 10016, USA (Tel. 212-889 0717)

Euroson '87: 6th Congress of the European Federation of Societies for Ultrasound in Medicine and Biology
June 14–18, 1987
Finlandia Hall, Helsinki, Finland
Further details. Congress Bureau, PO Box 824, SF-00101 Helsinki, Finland.

Ninth International Conference on the Use of Computers in Radiation Therapy
June 22–25, 1987
The Hague
Further details Organisation IX ICCR, Ir P. H van der Giessen, Dr Bernard Verbeeten Institute, P O Box 90120, 5000 LA Tilburg, The Netherlands, (Tel 013 655 725).

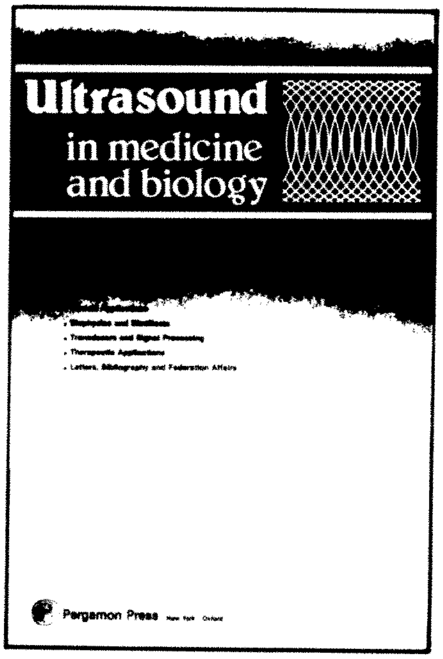
College of Radiographers' Annual Conference
July 1–3, 1987
Scarborough
Further details: Miss C. Aldridge, College of Radiographers, 14 Upper Wimpole Street, London W1M 8BN (Tel 01-935 5726, ext 206).

Blood Flow '87 (Techniques in blood flow measurement and their relevance to clinical diagnosis)
July 7–8, 1987
University of Leeds
Further details: Mr R Price, Department of Medical Physics, Leeds General Infirmary, Leeds LS1 3EX.

Fellowship Program in Diagnostic Ultrasound
July 1987–June 1988
Health Sciences Centre, Winnipeg
Further details Barbara Good, Course Co-ordinator, Section of Diagnostic Ultrasound, Health Sciences Center, 700 William Avenue, Winnipeg, Mb R3E 0Z3, Canada.

XI World Congress on Sarcoidosis and Other Granulomatous Disorders
September 6–11, 1987
Milan, Italy
Further details: PO XI WCS, Congress Studio, Via Cappuccio, 19, 20123 Milano, Italy.

1st Copenhagen Symposium on Uroradiology: Imaging and Interventional techniques
September 7–10, 1987
Herlev Hospital, University of Copenhagen, Denmark
Further details: Dr Henrik S. Thomsen, Department of Diagnostic Radiology 54E2, KAS Herlev, Herlev Ringvej, DK-2730 Herlev, Denmark.


Ultrasound
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ULTRASOUND IN MEDICINE & BIOLOGY

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New Patents Section — The journal now contains abstracts and illustrations of recently issued United States Patents and published patent applications filed from over 30 countries under the Patent Co-operation Treaty.
Software Survey Section — This new section reports developments in appropriate specialist software.

Subscription Information
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A selection of papers
Review paper. Contrast echocardiography, J ROELANDT.
Echocardiographic contrast patterns of the right-side of the heart: clinical significance, G GULLACE.
Contrast *M* -mode echocardiography in patients with interatrial communications, G KRONIK.
Videodensitometric processing of contrast two-dimensional echocardiographic data, R S MELTZER *et al.*
Comparison of methods of recording and analysis of Doppler blood velocity signals in normal subjects, S P CREEKMORE *et al.*
Method for estimating the Doppler mean velocity waveform, M S KASSAM *et al.*
A comparison of two calibration methods for ultrasonic hydrophones, W B GLOERSEN *et al.*
The concept of three dimensional resolution in echocardiographic imaging, L JOYNT & R L POPP.
Ultrasonic characterization of acute renal failure, V N GUPTA *et al.*
Measurement of soft tissue motion using correlation between A-scans, R J DICKINSON & C R HILL.
Oil-in-gelatin dispersions for use as ultrasonically tissue-mimicking materials, E L MADSEN *et al.*

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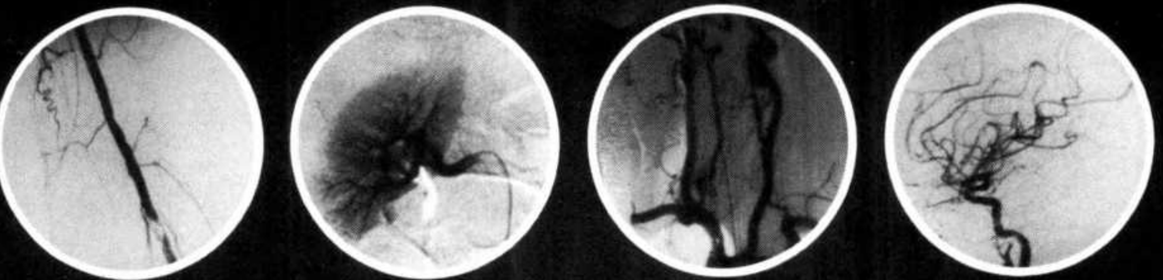

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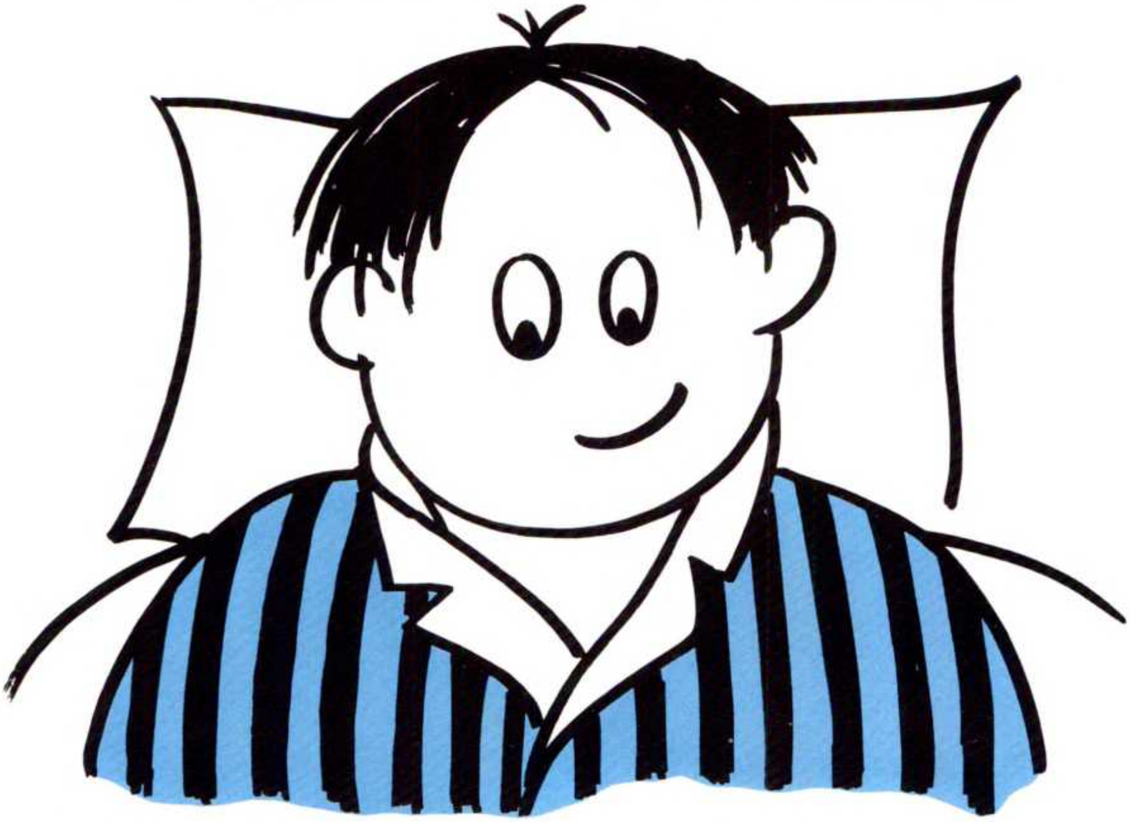

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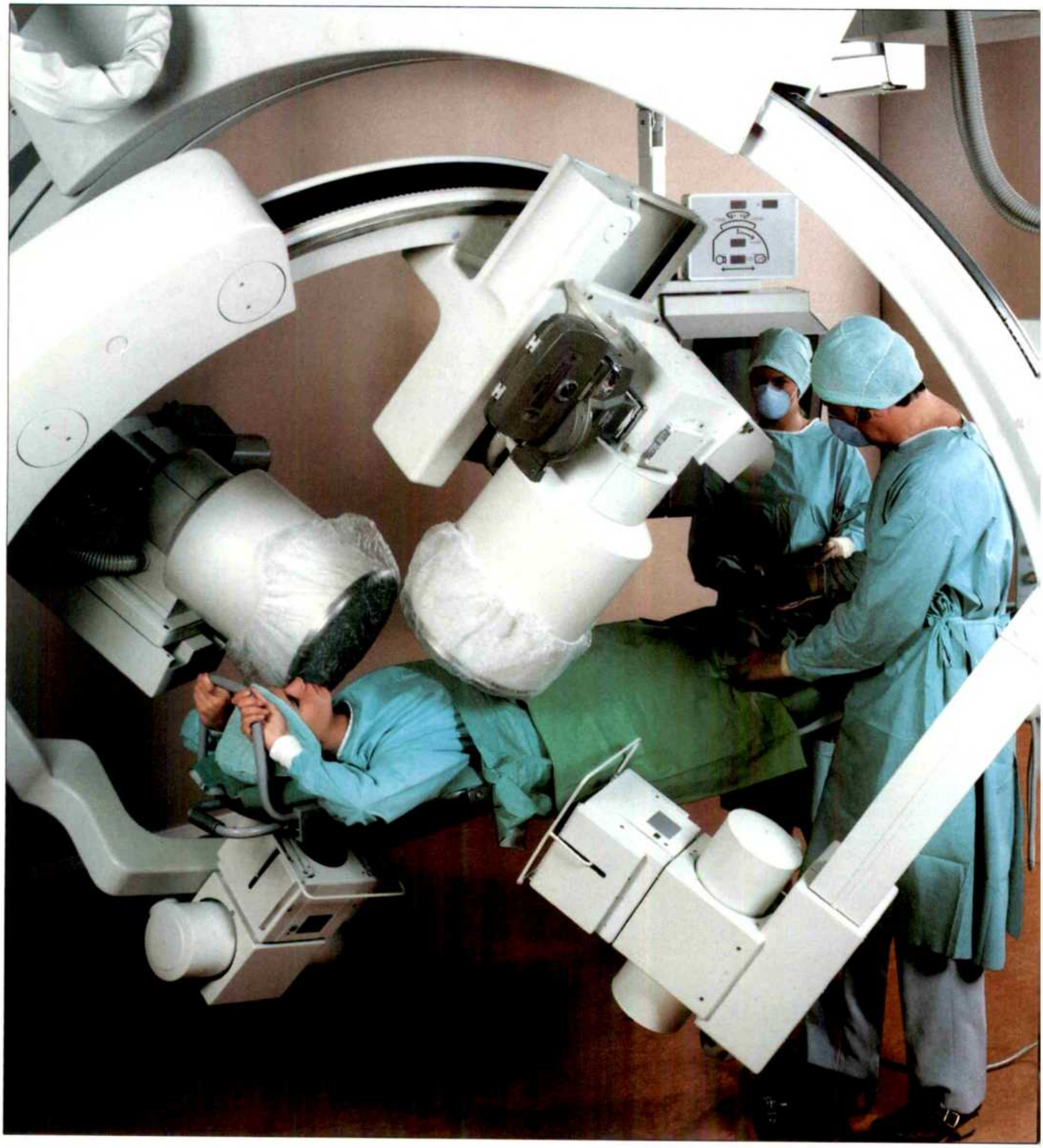

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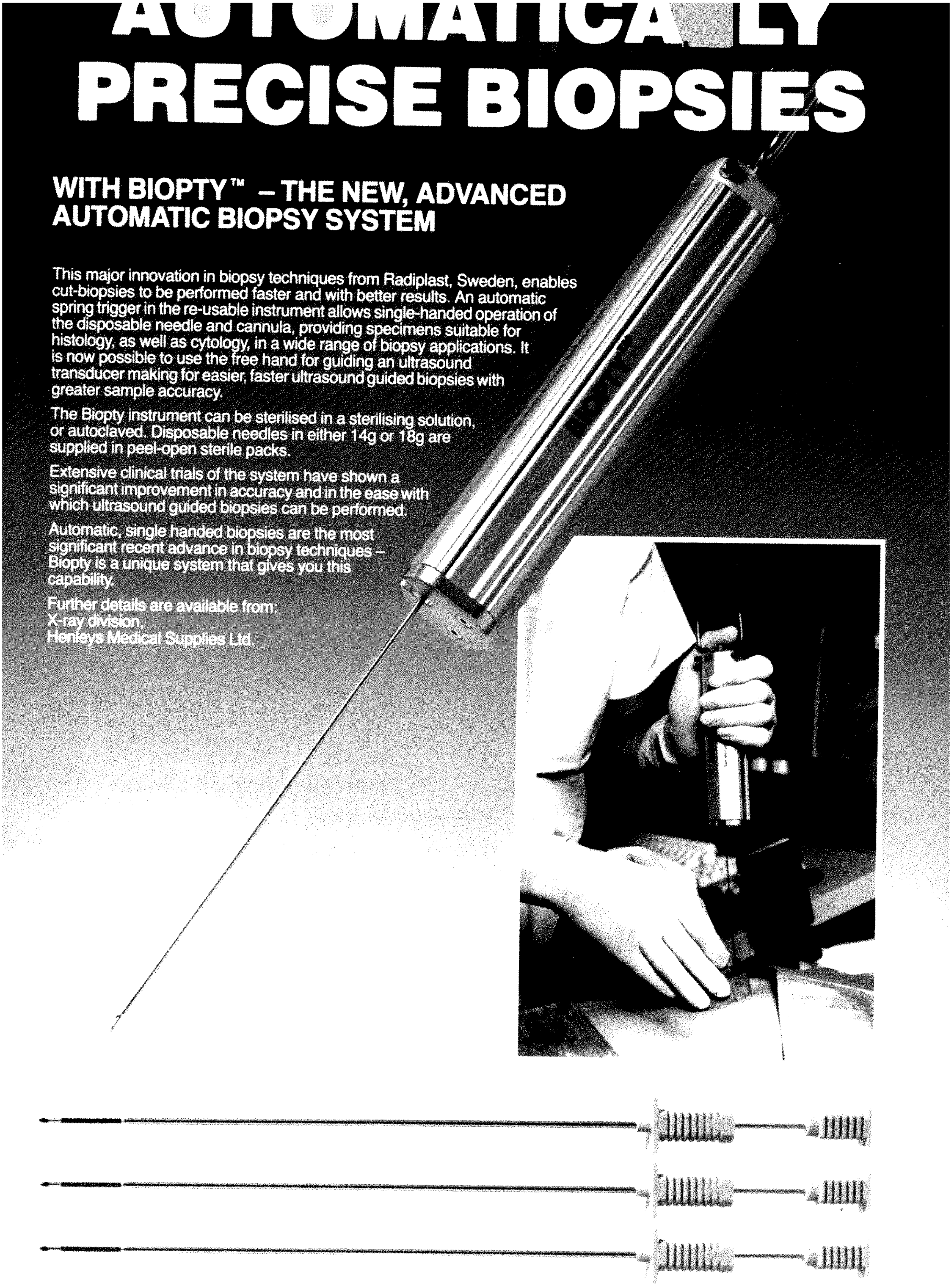

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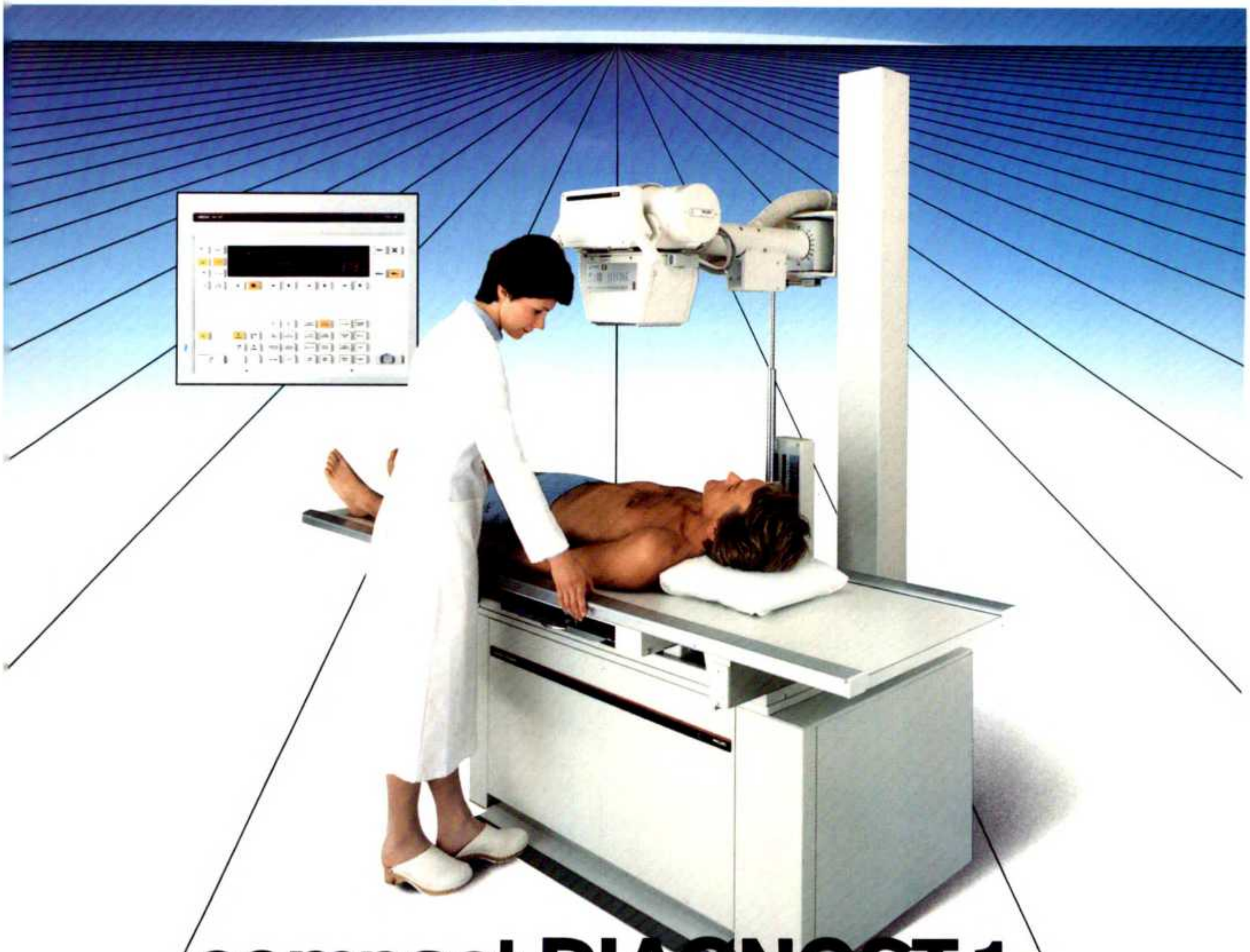

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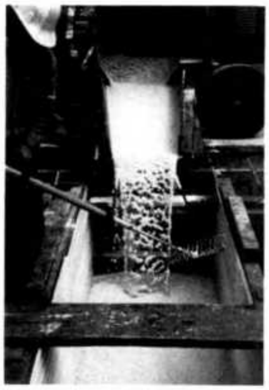

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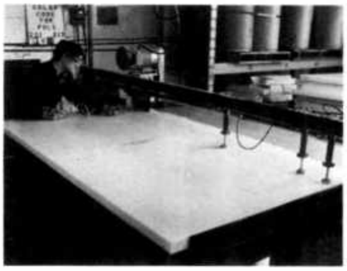

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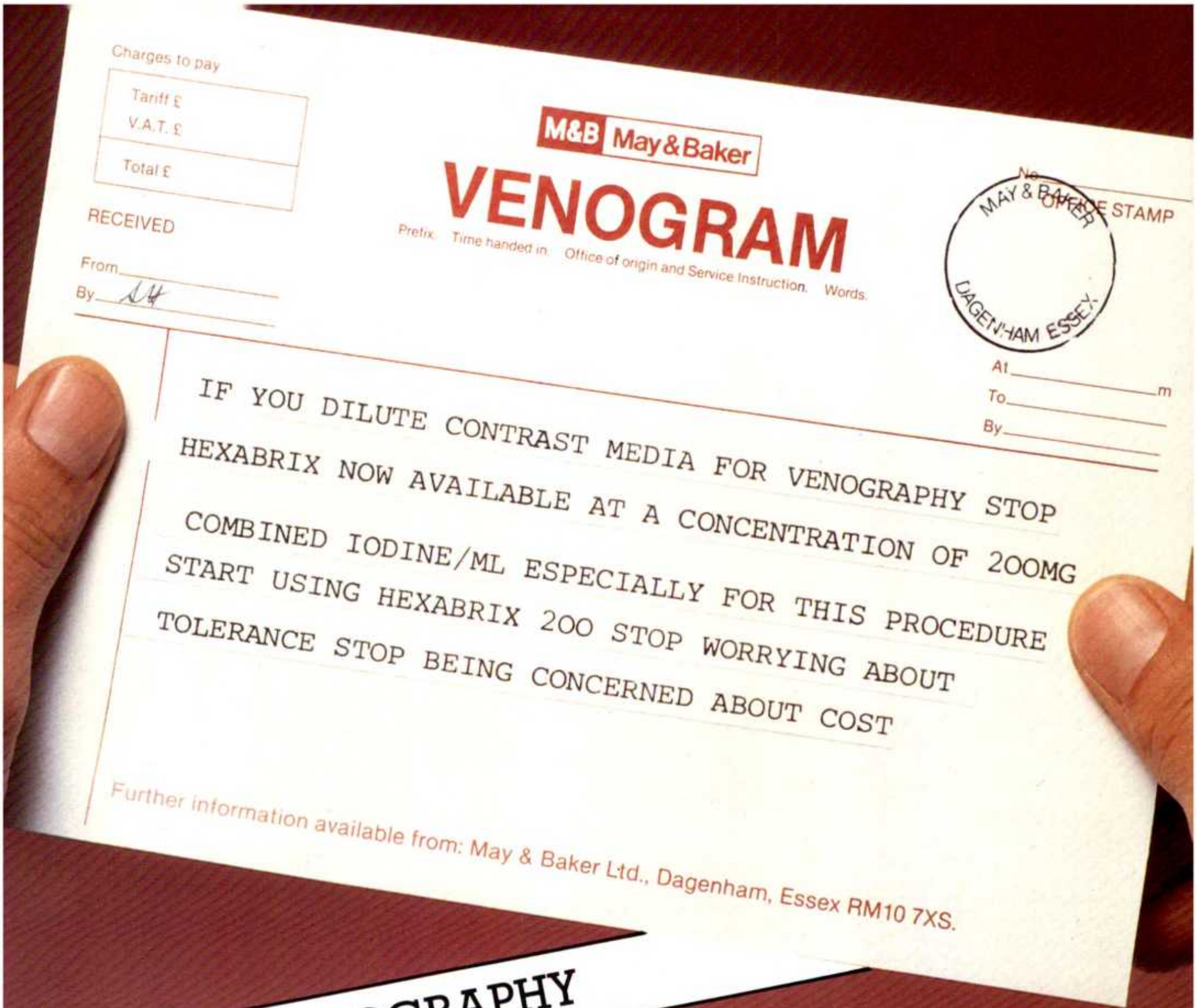

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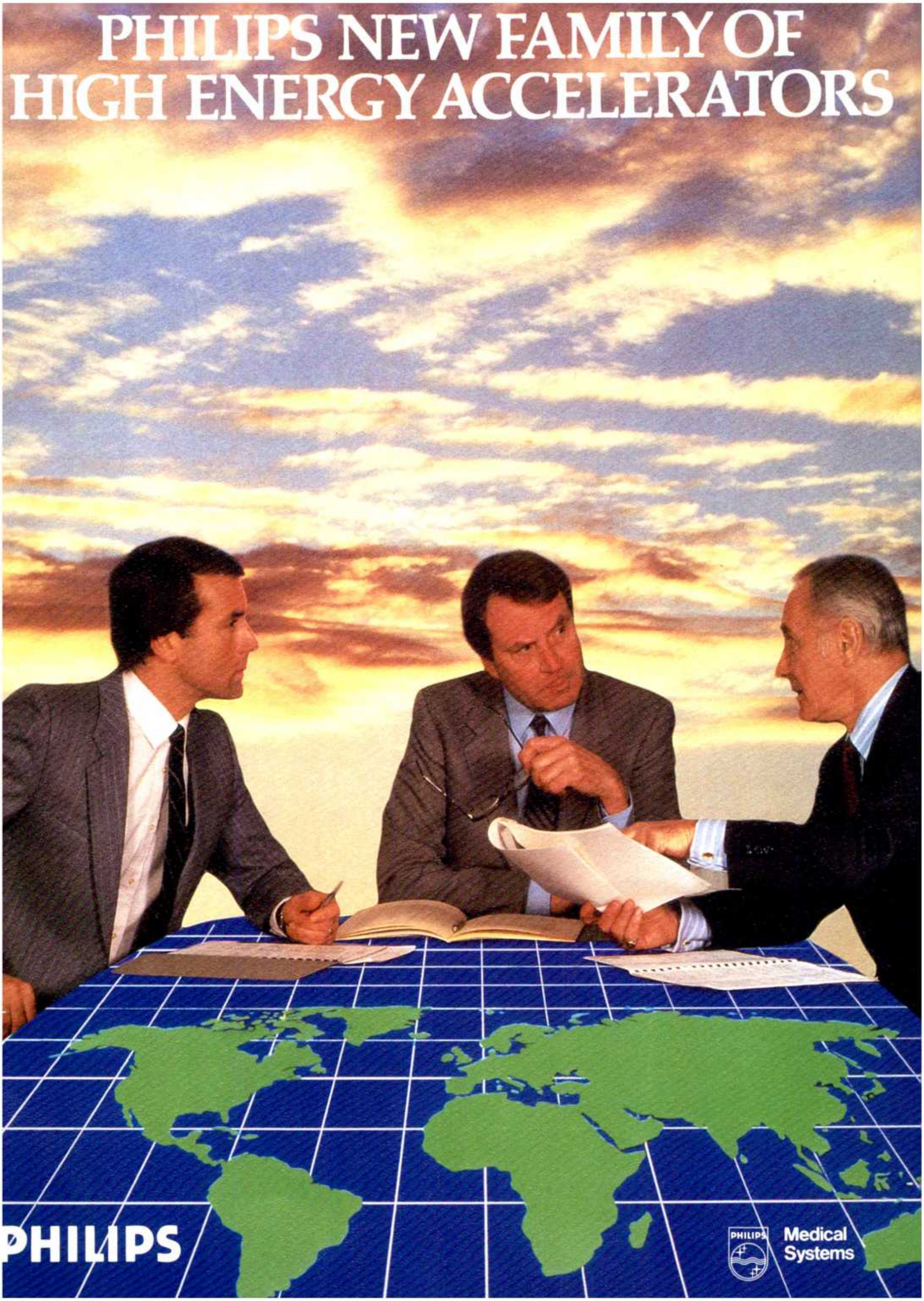

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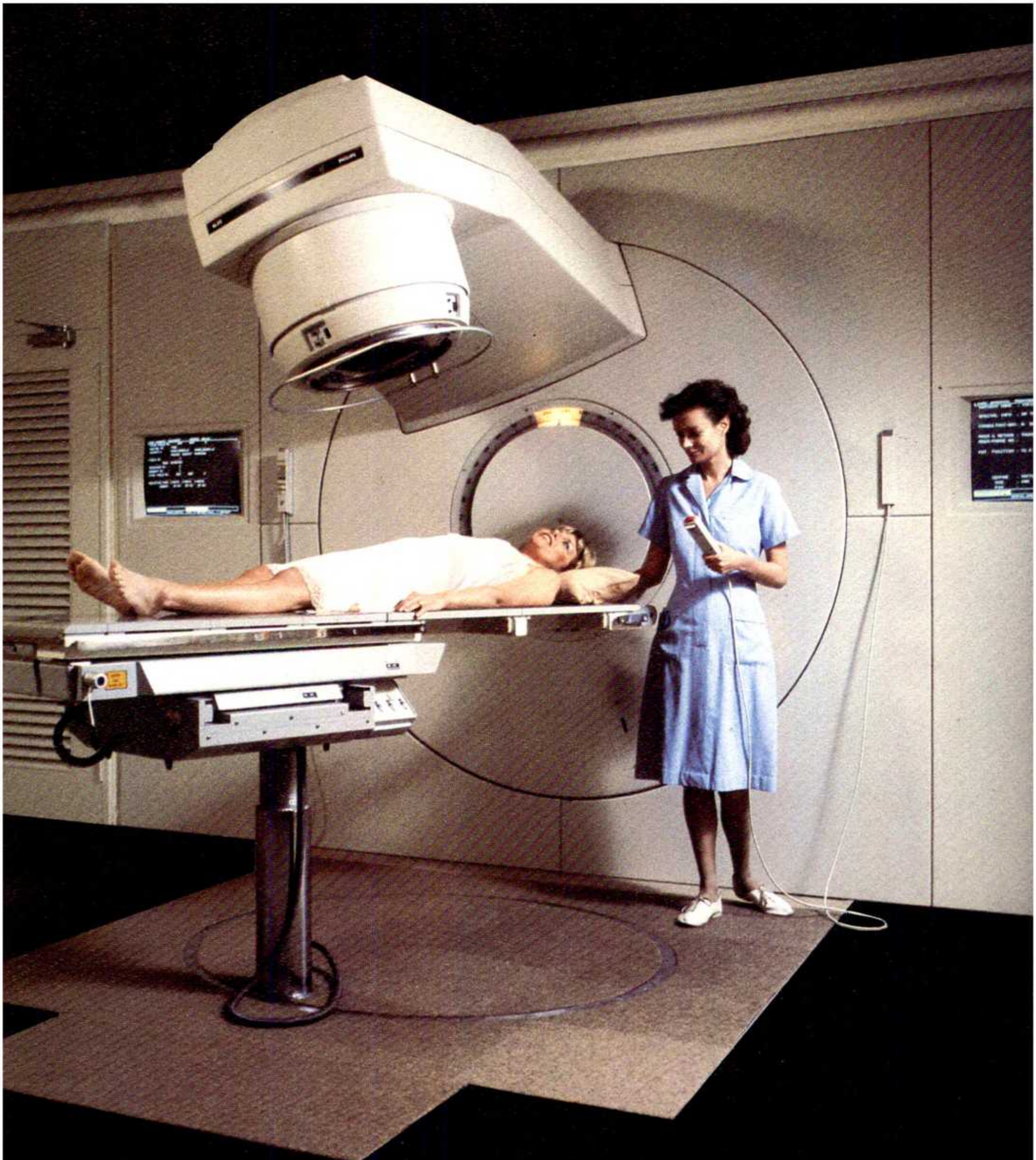

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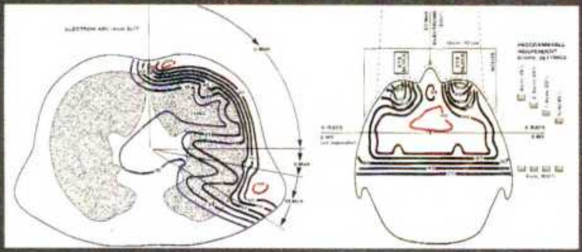

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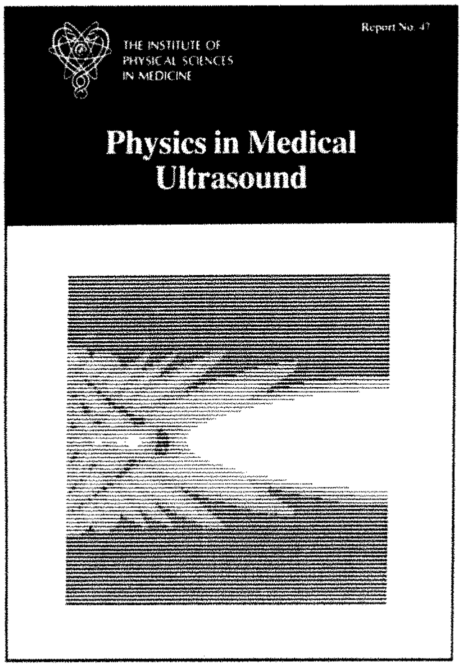
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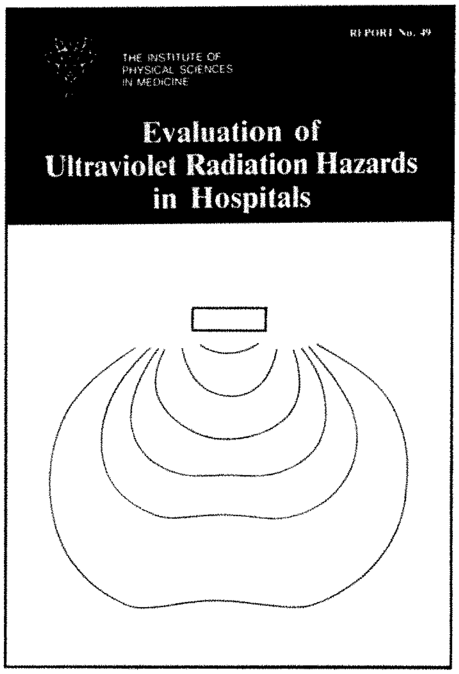
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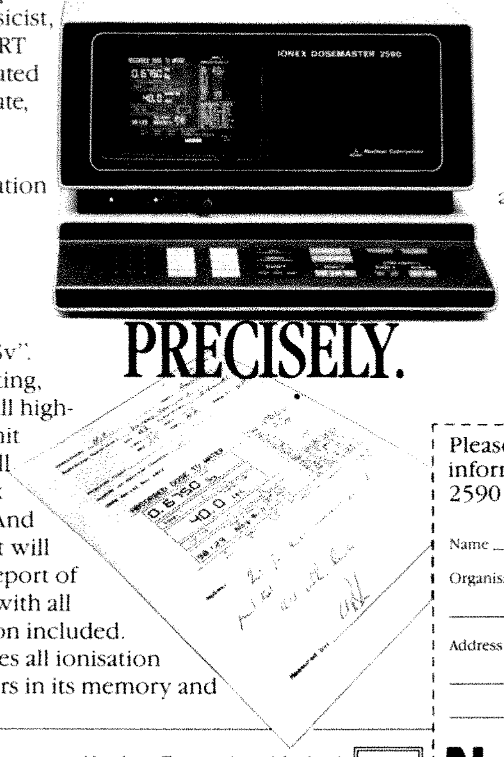

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The British Journal of Radiology

The prudent use of diagnostic ultrasound

British Institute of Radiology Presidential Address 1986*

By P. N. T. Wells, D.Sc., F.Eng.

Department of Medical Physics, Bristol General Hospital, Bristol BS1 6SY

(*Received May 1986*)

Abstract

Progress in diagnostic ultrasound is driven by the development of new technology. The place of new techniques in diagnostic algorithms has to be determined jointly by radiologists and clinicians and appropriate arrangements have to be made for training About £30 million per year is currently spent on diagnostic ultrasound in the UK. Diagnostic ultrasound depends on the information obtained as a result of ultrasonic irradiation of the patient Biological effects, some of which are undesirable, can be produced by ultrasound but there is no evidence that the exposures used in diagnosis carry any risk. In judging whether ultrasonic scanning is appropriate in any particular situation, it is necessary to consider benefits, costs and available resources. The costs include not only the costs of the test but also the cost of any hypothetical ultrasonic hazard and the cost of misdiagnosis. The most prudent use of ultrasound is that which maximises the benefit–total-cost ratio and although this cannot presently be quantified, some of the concepts involved can be understood in terms of the health increment and the health decrement, the latter apparently being equal to zero when the diagnosis is correctly made using contemporary equipment This approach can be extended to introduce the idea of profit arising from the test As an example, obstetric ultrasound is considered to be appropriate when there is a medical indication for it. Although routine scanning at 16 weeks of pregnancy has been shown to result in a very large profit, there is still conflicting guidance about its advisability on the grounds of safety and existing accounting systems may restrict access to the profit In discussing the desirability of ultrasonic scanning, patients can be informed that there is no reason to believe that there are any risks related to ultrasonic exposure The imminent availability of inexpensive ultrasonic scanners for the layman is a worrying prospect to which the medical profession should now try to develop a prudent response.

Michael Day, who was President of the Institute in the 1981–82 session, encapsulated the process of evolution in radiology when he said that "diagnostic procedures have been built into established clinical practice based on foundations laid by radiological pioneers" (Day, 1984). Moreover, the title of Day's Presidential Address, "Benefit and detriment in the medical use of radiation", was a timely reminder that ionising radiation at least is not without the potential to produce damaging effects; in diagnosis the detriment is always small, though there is scope for its reduction by improved techniques, and it should not contraindicate any examination with a measurable probability of benefit.

Economic pressures have escalated in medicine during the 4 years since Day considered benefit in terms of the sensitivity and selectivity of diagnostic tests and detriment in terms of radiation hazards. Nowadays, it is, more than ever, necessary to assess benefit by the effect which the result of the test has on the management of the patient; the detriment is measured by the financial cost of the test which includes not only the resources used but also a component equal to the value of the damage, including radiation damage to the patient, public and the staff, done by the test.

The prudent use of ultrasonic diagnosis depends on it being used cautiously, carefully, circumspectly, judiciously, sensibly and wisely. Like other technologies in medicine, diagnostic ultrasound is a resource which should be used with skill and good judgment. Jennett (1984) has pointed out that high-technology medicine is inappropriately deployed if it is unnecessary (because the desired objective can be achieved by simpler means), unsuccessful (because the patient has a condition too advanced to respond to treatment), unsafe (because the possible complications outweigh the probable benefit), unkind (because the quality of life after rescue is not good enough, or long enough, to justify the intervention) or unwise (because it diverts resources from activities that would yield greater benefits).

Nowadays, ultrasound has become established as a diagnostic tool in many different medical specialties, particularly obstectrics, internal medicine, urology, cardiology, gynaecology and vascular diseases. Sometimes its benefit is obvious. Often, however, the benefit presently is not judged in relation to the detriment and it is here that the question of prudence needs to be considered.

THE IMPACT OF NEW TECHNOLOGY ON RADIOLOGICAL PRACTICE

Although it is desirable that the potential social effects and short-term and long-term consequences of new technology should be systematically assessed before the technology becomes available (Banta et al, 1978), the pressure to obtain the "benefits", whether imaginary or real, of new technology is usually too great for this to be realistic.

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*Delivered at the meeting "Safety of ultrasound", held at the Middlesex Hospital Medical School, London, May 15, 1986

Progress in diagnostic ultrasound, as in other areas of radiology, is driven primarily by the development of new technology. Generally, a new radiological technology is not initially developed as a solution to a previously identified problem, rather, a new type of instrument is first constructed and then the radiologists set about the task of demonstrating what radiological problems it can be used to solve. Moreover, the life of any viable new technology has four phases: the idea, the adoption of the technique, its acceptance and, finally, its decay into disuse, although the actual lifetimes of different technologies may be very different.

Progress in diagnostic technology is one of the factors which has led to the increase in the average severity of illness in hospital, and to the increase in hospital costs, as clinicians treat less critically ill patients in ambulatory settings. Although it is, paradoxically, true that the contribution of technology to overall costs is small in comparison with the costs of increasingly complex surgery (Showstack et al, 1985) and that a 50% reduction in the provision of expensive technologies would cut less than 1% off total health expenditure (Maloney & Rogers, 1979), the problem of financial constraint and the pressure to reduce radiation exposure mean that new radiological technologies can only be introduced into clinical practice if they replace older procedures. A patient with a given set of signs and symptoms must not be exposed to a battery of radiological tests, some of which may be unhelpful. Rather, it is necessary to develop new sets of algorithms that are flexible, related to clinical manifestations, to the institutions and to locally available equipment and clinicians (Margulis, 1981). These algorithms have continuously to be reviewed and, if necessary, modified by radiologists and clinicians working together. Properly used, this approach results in optimal benefit being gained from the introduction of new radiological technologies; otherwise, new technologies can be blamed for the disappointment of unfulfilled expectations.

The performance of a diagnostic test in terms of sensitivity and specificity in relation to a particular disease is often too rigorous a concept in judging the role of the test in an algorithmic approach. In a well designed algorithm, the test carried out at each step needs only to provide the answer to a relatively simple question. This is shown in Fig. 1, which illustrates the diagnostic algorithm for patients with signs and symptoms of renal disease. Ultrasonic scanning is the first test, and what follows is determined by whether the scan appears to be normal or abnormal. Notice that interventional treatment, such as cyst aspiration and cytology, only follows directly from a test known to be highly sensitive and specific to the condition diagnosed. Otherwise, the result of the test serves to decide on the subsequent, more appropriate, but perhaps more expensive or invasive, test Notice, too, that there is an element of redundancy in the algorithm so that the same conclusion can be reached by travelling along different pathways.

In fact, the clinical history is generally the most important factor in both diagnosis and management Unnecessary tests are a significant waste of health resources (Sandler, 1979) and radiologists are now rightly trying to limit the use of radiology to situations in which it really is useful (Fowkes et al, 1986).

Another important aspect of the arrival of a new radiological technology is that diagnostic staff have to be trained in its use. The pioneers are self-trained; they are usually enthusiasts and, at least for the new technology, their skill is technology- rather than system-based. As the technology becomes diffused, during the adoption and acceptance phases of its clinical life, the radiologists who use it routinely are nowadays generally

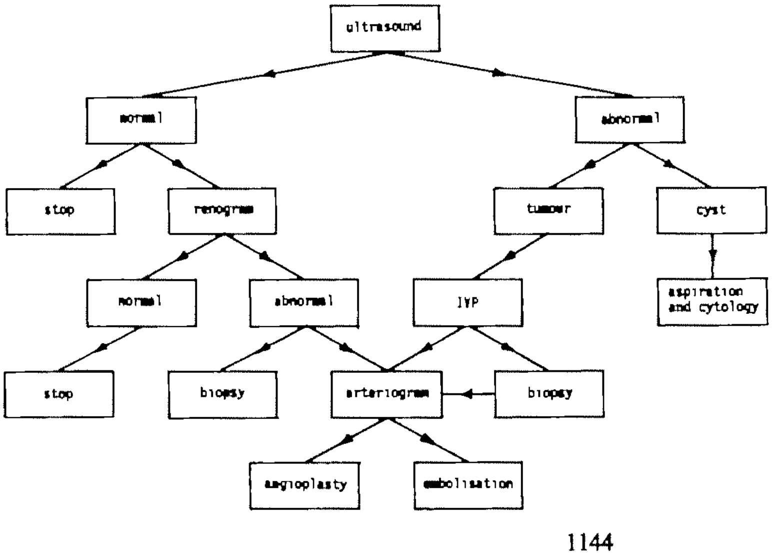

FIG. 1
Diagnostic algorithm for patients with signs and symptoms of renal disease

system-based and the radiographers are technology-based so they need additional training and periodical refreshment and updating. Although this is demanding, it is part of what makes radiology both challenging and fun.

RADIOLOGY AND THE ROLE OF DIAGNOSTIC ULTRASOUND

In the UK presently, about £200 million is spent annually on diagnostic radiological services, equivalent to 1.3% of the resources allocated to hospitals. There are just short of 1000 consultant radiologists, one out of every 15 consultants. A reasonable estimate is that ultrasound accounts for 15% of the radiological workload.

The £30 million devoted to diagnostic ultrasound each year covers the costs not only of staff salaries and training but also of equipment acquisitions, maintenance and quality control. It also includes the costs of a relatively small number of diagnostic ultrasound examinations not carried out in radiology departments, principally in obstetrics, cardiology, ophthalmology and vascular studies.

THE SAFETY OF DIAGNOSTIC ULTRASOUND

Ultrasound is capable of affecting biological tissues and some such interactions would be undesirable if they were to occur in human diagnostic investigations. The possible mechanisms of interaction are thermal, mechanical and indirect. Thermal effects depend on the heat produced as a result of the absorption of ultrasound Mechanical effects are due to forces resulting from streaming velocity gradients which may be amplified in the presence of cavitation bubbles of appropriate dimensions. There is evidence that some biological effects occur that cannot be explained in terms of thermal or mechanical interactions; more research is needed to identify such indirect mechanisms.

If one thing is clear to a student of the literature on the bioeffects of ultrasound, it is that no systematic pattern of directed research has emerged. The available data consist of the results of experiments carried out by independent investigators over a long period of time; moreover, only a few of the investigators have the necessary knowledge of physics and biology to have published fully satisfactory information. Indeed, much of what has been published is merely distracting because of the failure of the experimenters to understand key aspects of the work.

Ultrasonic diagnosis depends on the information obtained as a result of ultrasonic irradiation of the patient. If the exposure is too low, useful information is not obtained; if it were to be too high, harm to the patient could result. (It is a fact that the exposures presently used in ultrasonic diagnosis are determined not by scientifically established levels related to risk, but by the amount of energy convenient for equipment design for good diagnostic performance.) To judge the risk of harm, it is necessary to know the ultrasonic exposure conditions. Preston and Hill (quoted in the Medical Research Council (1986) report) recommended that the minimum parameters for which operating values should be reported are: frequency; spatial-peak temporal-peak positive and negative pressures; spatial-peak temporal-average intensity, and, for Doppler equipment only, the 6 dB beam area in the focal plane.

It is impossible to prove safety by showing negative effects, but the establishment of understanding of underlying biophysical mechanisms of interactions may allow attempts to be made to define safe exposure conditions. Another approach is to relate the exposure conditions used in diagnosis to exposure conditions known to produce biological effects and, thus, at least to be able to say whether or not the diagnostic exposure is "potentially harmful". This was first done by Ulrich (1971, 1974) and by Wells (1974) by reference to simple charts of ultrasonic intensity versus exposure time, and the idea was developed to form the basis of such guidance as that of the American Institute of Ultrasound in Medicine (1984). The usefulness of charts can be extended by including additional variables: Fig. 2 shows an attempt to do this for intensity, pulse length and exposure time. In this chart, the exposures for physiotherapy are believed to produce (beneficial) biological effects, while those for Meniere's disease therapy and above the threshold for neural tissue lesion induction produce real damage. Clearly, some *but not all* parameters for each of the different types of diagnostic exposure (pulse echo, pulsed Doppler, and continuous-wave obstetric and peripheral vascular Doppler) exceed those of exposures believed or known to produce biological effects.

A British Institute of Radiology report (in press) is one of several conscientious attempts to examine the scientific data relating to the safety of diagnostic ultrasound. This document begins with a review of exposure conditions presently used in diagnostic ultrasound and this is followed by sections dealing with biological effects reported following exposure to diagnostic ultrasound, the effects of ultrasound at diagnostic intensities on animal reproductive tissue, the biological effects of high-level ultrasound of relevance to diagnostic exposure conditions, and human epidemiological data. No evidence has been found even to suggest that present ultrasonic diagnostic practice carries any hazard due to the ultrasound.

As far as ultrasound is concerned, there is no equivalent to the concept of collective dose of ionising radiation as an indicator of the total harm to society, presently costed at £3000 per man-sievert at the baseline but increasing non-linearly with increasing individual exposure (National Radiological Protection Board, 1985).

JUDGING BENEFIT AND DETRIMENT

Benefit in relation to premium

Roberts et al (1985) demonstrated that the UK National Health Service could afford to spend £14 000

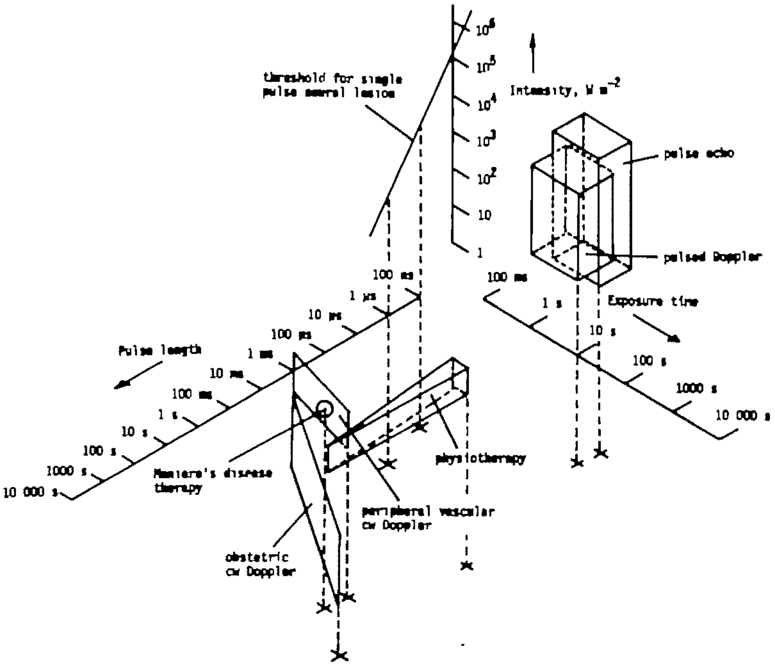

FIG. 2.
Chart showing exposure conditions (peak ultrasonic intensity, ultrasonic pulse length and total time) for various diagnostic techniques and for typical therapeutic applications

to save a life or to avoid a long-term disability in 1981–82. This figure does not depend absolutely on the intrinsic value or quality of life but is fixed by the cash available to be spent by the NHS on acute medical care and preventive screening services, which is, of course, determined by the resources allocated by government, and the benefit–premium ratio, which is determined by the incidence of relevant health demand in the community. The cost of any life-saving or disability-preventing patient management scheme in excess of £14 000 has either to be offset by schemes costing less than £14 000 per patient or by limiting the availability of other schemes. It is worth noting that society's valuation of life-saving depends on the perception of the risk (Cohen, 1980). For example, the estimated cost per fatality prevented (in 1975, US dollars) ranges from $20 000 spent on road maintenance, through $250 000 for seat belts to $10 000 000 for the general disposal of radioactive waste; in contrast, increase in the availability of immunisation in Indonesia, for example, would cost $100 per life saved. Consequently, spending more or less than £14 000 on a life-saving or disability-preventing patient management scheme in the UK is not necessarily bad or good: citizens simply have to judge whether the balance of the cost of health-care provision is what they want within the available resources—and that the total available resources are also what leaves them feeling least uncomfortable, and that is really what the government is judging when it puts its cash limit on the NHS.

This discussion is actually quite relevant to the prudent use of diagnostic ultrasound in routine clinical situations. For example, the financial cost of avoiding a handicapped survivor with open neural-tube defect when the population prevalence is 1.25 in 1000 by any effective fetal screening programme involving ultrasound ranges from £38 000 to £51 000 at 1980 prices (Hibbard et al, 1985) and this may well be judged to be more than the NHS can afford (even though the undiscounted excess lifetime costs to society incurred by such a survivor have been estimated at £118 000). Thus, screening for neural-tube defects may not be a "prudent" use of diagnostic ultrasound. Later on, however, a more simplistic accounting, rather than insurance, approach to the analysis of this situation is discussed which seems to dispel any such doubt. A seemingly irrational practical problem may remain: this is that existing accounting systems may preclude the savings made as a result of routine scanning from being available to cover the cost of the scanning.

The cost of an ultrasonic examination

It is not easy to calculate the real cost of any diagnostic radiological procedure. The costs of staff, equipment, disposables, nursing, clerical work, portering, transport and accommodation need to be taken into account. On this basis, a 20-min ultrasonic examination must cost about £15. A prudent clinician might think that £15 could be saved by not requesting such a scan for a particular patient. Unfortunately, however, the only expenditure not incurred by the radiology department by not doing the scan is the cost of the consumables, equal to about £2, since the other facilities have to be paid for whether they are used or not. ("Vire-ologist" (1986) has suggested that this potential pitfall in clinical budgeting might be avoided by presenting the cost of any requested investigation as the total cost and the variable (or "vireable") element of it.) The full savings can only be achieved by the health authority if the "size" of the radiology department can be reduced in response to falling demand. This option is likely to be unattractive to radiologists. It is pertinent to note that a computed tomography examination typically costs about £120 and a magnetic resonance imaging examination about £250. The vireable elements of these investigations may be as little as £10 and £15, respectively. Thus, it is clear that significant savings can be made in radiology departments only by totally eliminating one or more "big-ticket" facilities, or by real reductions in staff establishments. Ultrasound is generally a "little-ticket" study and if it can provide useful information in any particular clinical problem its use is likely to be "prudent" in terms of cost-effectiveness.

The implications of misdiagnosis

Tuddenham (quoted by Kundel & Hendee, 1985) suggested that one very important area of investigation is the determination of the true societal cost of missed radiological diagnosis. If lesions missed in radiology should turn out to be unlikely to be detected by history, physical examination, laboratory studies, endoscopy and so on, there would be convincing evidence that research is needed in this area. But if it were to be impossible to demonstrate that missed radiological diagnoses lead to disability, death and increased health-care costs in a significant number of cases, the whole issue could be laid to rest.

It has recently been recognised that clinical care of patients may often be described in terms of a *cascade*; the process, once started, proceeds stepwise to its full, seemingly inevitable, conclusion (Mold & Stein, 1986). The chain of events tends to proceed with increasing momentum, so that the further it progresses, the more difficult it is to stop. The participants in the process are often unaware that it is a cascade effect. Anxiety on the part of the clinician is frequently an important factor fuelling cascades. Radiology, even ultrasound, may be one step in a cascade which, at best, results in a correct diagnosis leading to an appropriate next step but which, at worst, leads to a misdiagnosis with the possibility of a bad outcome for the patient.

Examples of potential errors in ultrasonic diagnosis which may propagate unwanted or harmful cascades include: overdiagnosis of fetal abnormality, leading to termination of a normal, wanted pregnancy; failure to detect hepatic secondary neoplasm, leading to inappropriate treatment such as laparotomy; and underdiagnosis of carotid artery disease, leading to failure to offer appropriate treatment and the consequent occurrence of stroke. Some errors in ultrasonic diagnosis are due to inadequate equipment and some are due to inadequate training or experience. Prudence demands that ultrasonic examinations should be carried out by well trained people using adequate equipment. Perhaps the least prudent use of diagnostic ultrasound is when people with inadequate training perform the examination or interpret the results.

Health increment and health decrement

Ultrasonic diagnostic procedures carry no radiation risks for the public or for the careful operator; it is evident that radiation protection analogous with that necessary with ionising radiation is not required. Most people seem to feel intuitively that the ultrasonic exposure to the patient should be subject to the ALARA (as low as reasonably achievable) principle. The ALARA principle takes economic and social factors into account (International Commission on Radiological Protection, 1983) and does not equate to any system of control that simply requires everything possible, or technically feasible, to be done to reduce doses without consideration of the cost, the magnitude of the benefit from the dose reduction, or any other aspects. In the case of ultrasound, however, for which there is no evidence of detriment due to exposure such as that due to the contribution of medical radiography to the population dose, the most *prudent* use of ultrasound is arguably that which provides the maximum benefit–total-cost ratio. This rather new idea is a development of older principles. For example, the National Council of Radiation Protection and Measurements (1983) recommended that "users should strive to obtain the most medically significant information possible while producing the least ultrasonic exposure to the patient. By the latter is meant, specifically, that dwell times and total exposure times should be minimised and, where adjustable, intensities should also be minimised". Unfortunately, this approach leaves matters to the judgment of the user without giving satisfactory quantitative criteria. Obviously, as the ultrasonic exposure is progressively reduced, the diagnostic information is first degraded and eventually lost altogether. As the intensity is increased, generally more diagnostic information becomes available, but biological damage is suffered by the irradiated tissues. (Paradoxically, above some level of intensity, the value of the diagnostic information begins to decrease, partly because of such effects as non-linearity and partly because the information obtained reflects the damage done by the ultrasound.) Nyborg (1985) recognised this and suggested that ultrasonic exposure conditions should be optimised, rather than simply being subject to the ALARA principle. He proposed that the exposure conditions should be chosen to give the maximum (health increment – health decrement) difference, or at least a positive value for this difference, where the *health increment* is the value to the patient and the community of the benefit of the test and the *health decrement* is the cost of the damage done to the patient by the ultrasonic exposure. Although, conceptually, a significant step forward, this approach is not without its difficulties. Presently, it is impossible to place financial values on the health decrement of the ultrasound exposure, and it is very difficult to evaluate the health increment of the diagnostic information. Since there simply is no evidence that contemporary ultrasonic diagnostic procedures carry any hazard, the value of the health decrement is apparently zero (assuming a correct diagnosis) and certainly it is very small in relation to the cost of carrying out the test. The health increment depends on the clinical situation and, just as with radiographic diagnosis, it needs to take into account the increase in both the duration and the quality of the life of the patient resulting from management decisions taken as the result of the test.

Figure 3 is an attempt to put these considerations into perspective, on the assumption that the test always produces the correct diagnosis. Of course, the data in this figure are hypothetical and have been rather unrealistically chosen insofar as a substantial health decrement is represented with increasing intensity beginning towards the low end of the range of intensity, giving a health increment. There are two important points to note Firstly, the maximum value of the health-increment–cost ratio is not much reduced by taking the health decrement into account and in practice there is no need to choose the intensity carefully to maximise this ratio because the maximum health increment is approached at an intensity well below that at which health decrement begins. Secondly, the health-increment–health-decrement ratio is not a helpful index of whether the test is worth carrying out, because it does not take into account the fixed cost of the test (*i.e.* the value of the resources used to obtain the health benefit). Essentially, the health-increment–health-decrement ratio is relevant to the ALARA principle, while choosing the intensity to maximise the health-increment–total-cost ratio ensures the optimal use of resources. If the health-increment–total-cost ratio exceeds unity, the test is apparently justifiable, since the *output* then exceeds the *input* and a *health profit* has been achieved. Notice that the data for a real test would need to include a component allowing for diagnostic errors. It is also important to note that even when it becomes possible, if it ever does, to quantify increment and benefit to the extent that profit can be calculated, the optimisation of the use of health resources will depend upon any procedure (including diagnostic tests) which is made available clinically having a profit margin, expressed in percentage terms, which exceeds the minimum ultimately determined by the politically perceived expectations of the community.

Factors such as public pressure, political concern and economic interest have to be taken into account in making decisions about the allocation of resources. Such factors are transient, unpredictable and involve value judgments. If they are incorporated into mathematical formulations of increment and detriment, they need to be identified and distinguished from

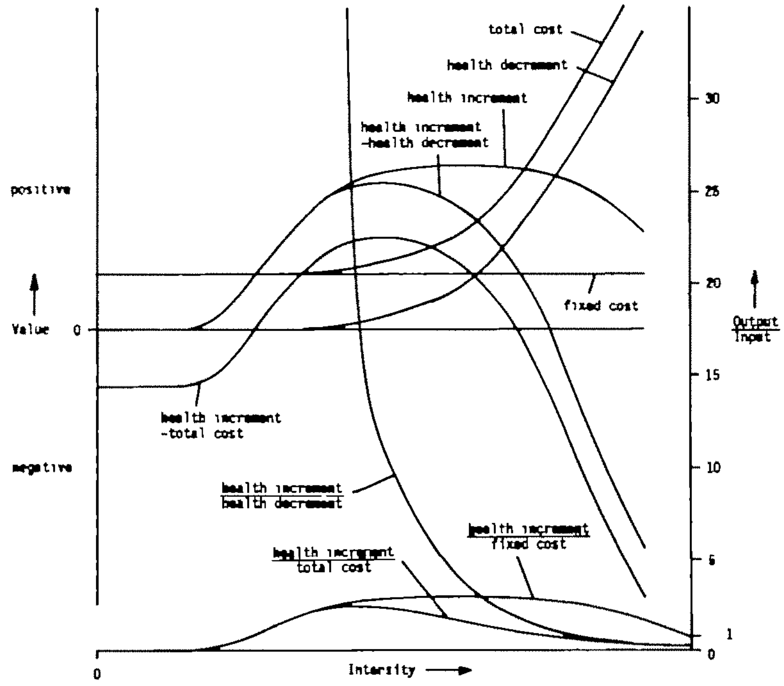

Fig. 3.

Graph showing general relationships between the value of an ultrasonic diagnostic test and the ratio of the output value to the input value, as functions of the ultrasonic exposure expressed as the peak intensity. The test is assumed always to result in the correct diagnosis provided that the itensity is within the range that provides adequate information. The data are hypothetical and health decrement illustrated as being due to high intensity is much greater than would occur in practice.

measurable physical quantities such as salaries, equipment costs, maintenance, consumables and accommodation.

AN EXAMPLE: PRUDENCE IN OBSTETRIC ULTRASOUND

The National Institutes of Health (1984) organised a Consensus Development Conference which identified 28 clinical conditions, ranging from estimation of gestational age to evaluation of fetal condition in late registrants for pre-natal care, in which the use of diagnostic ultrasound may be medically indicated in pregnancy. When there is a medical need for such an examination, it is prudent to go ahead with it. Apart from the commitment of resources, the only obvious risk is that of misdiagnosis. At present, one of the most important risks is that of inappropriate termination of pregnancy and, in this connection, it is important to remember that recent advances in neonatal surgery are potentially able to treat many urinary-tract abnormalities, gastroschisis, isolated exomphalos, diaphragmatic hernia and gastrointestinal anomalies. In such cases, termination on the basis of ultrasonic fetal detection may be unjustifiable (Brereton, 1984). Worst of all for the individual, of course, is the termination of a normal pregnancy in which fetal abnormality has been wrongly diagnosed by ultrasound.

The use of ultrasound for routine screening in pregnancy is controversial. One of the main reasons for concern is the numbers of fetuses involved, amounting to more than 700 000 in the UK every year, with an already low rate of poor perinatal outcome. The position of the Royal College of Obstetricians and Gynaecologists (1984) is that "there are cogent reasons to expect benefit to all mothers and babies from a well performed scan between 16–18 weeks of pregnancy, but there is need for a large well planned prospective study to determine the extent of the benefits of routine scanning over selective scanning on medical indication". The European Federation of Societies for Ultrasound in Medicine and Biology (1984) has stated that "routine clinical scanning of every woman in pregnancy is not contraindicated by the evidence currently available from biological investigations and its performance should be left to clinical judgement". The National Institutes of Health (1984), however, have concluded that "data on clinical efficiency and safety do not allow a recommendation for routine screening at this time".

Faced with this conflicting advice, what is the radiologist to do? It is well known that the usual risk factors for intrauterine growth retardation (IUGR) are rather non-specific, since only about half the babies who are small for dates are born to mothers with these risk factors (Neilson, 1979). It has been demonstrated (Neilson et al, 1984) that a two-stage screening schedule (consisting of an ultrasound examination before 24 weeks to establish gestational age, followed by a second examination at 34–36 weeks to determine the product of the fetal crown-to-rump length and trunk-area) has high sensitivity and specificity in identifying small-for-dates fetuses. The controlled trial, limited to 1533 single pregnancies, failed to demonstrate any benefit, in terms of management or outcome, from applying the two-stage ultrasound schedule to low-risk pregnancies. This result, however, strengthens the arguments for having a routine scan of every pregnancy before 16 weeks, for not only can fetal abnormalities be detected then and appropriate action taken, but also the determination of gestational age can be a great help in the subsequent management of difficult pregnancies, including those with IUGR (Whitfield & Neilson, 1984).

In an evaluation of the cost–benefit of carrying out a scan at about 16 weeks for all pregnancies and using his own financial estimates, Campbell (quoted in the Medical Research Council (1986) report) showed that routine scans detected 50 abnormalities in 14 622 deliveries; eight abnormalities had remained undetected and there had been one false positive scan. Of those detected, seven abnormalities would have been predicted to result in severe handicap such that the cost of caring for the handicapped individuals over 40 years of life would have been more than £2.5 million. The total costs of the single routine scans were calculated to be about £150 000. Seen simplistically from this accounting viewpoint (as opposed to the insurance viewpoint of Hibbard et al (1985), previously discussed), the profit due to routine scanning was more than 1500%! Although the justification for a second routine scan at 32 weeks is less convincing, the evidence does seem to amount to proof that routine scanning in pregnancy is prudent, given the present prevalence of fetal abnormalities and the inappropriateness of alternative screening methods, but *only* provided that the screening is carried out by adequately trained and skilled staff. These figures are, of course, more dramatic than those of Hibbard et al (1985) mentioned earlier, because they are based only on one inexpensive scan per patient and no biochemical or other tests. Moreover, if in practice the necessary fraction of the savings cannot be made available to cover the costs of scanning, the service cannot be provided—and that does not seem to be prudent accounting.

THE PRUDENT INVOLVEMENT OF THE PATIENT

In discussing the advisability of having an ultrasonic scan, the doctor should explain the anticipated benefit of the test to the patient, whether this is to screen for asymptomatic disease, leading to earlier detection and more effective treatment, to help to diagnose disease, leading to appropriate treatment, or to assess the extent of disease, leading to more sensible management. In relation to the examination procedure, the question of safety should be addressed together with such aspects as comfort, time, preparation and cost. Patients should be informed that there is no reason to believe that ultrasonic diagnosis has any risk related to ultrasonic exposure. If untoward effects are occurring, they are so rare as to be unnoticeable or so subtle as to be imperceptible.

THE LAYMAN'S SCANNER: A WORRYING PROSPECT

Now that liquid-crystal image display devices of good quality have become available, it is inevitable that a new class of inexpensive real-time scanners will soon begin to appear. Probably the first of these instruments will be designed for use by clinicians and general practitioners: they may be pocket-sized and battery-operated and, if used responsibly, they should allow straightforward investigations to be carried out in the office, clinic or ward. Consequently, patients referred to radiologists will be likely to be mainly those with non-trivial problems requiring an expert approach to diagnosis. Since ultrasound appears to be safe, this can only be considered to be a good development in the practice of medicine.

The next stage in the evolution of this technology will likely be the appearance of scanners aimed at the consumer market. The cost of such "layman's scanners" will primarily be determined by the size of the market and it is conceivable it could be as little as £100. It is no good to hope that this challenge to conventional medicine will disappear simply because it is worrying to doctors! There seems to be no scientific basis for proposing that cheap scanners should be prohibited by regulations, or made available only on prescription! The position of the Royal College of Obstetricians and Gynaecologists (1984) is that "commercial exploitation of antenatal scanning by poorly trained personnel merely to let parents 'see the baby' is to be deplored". All that can be said at the moment is that the medical profession should now try to develop a prudent response to the inevitable.

CONCLUSIONS

Every model of medicine begins with diagnosis, implicit in which is prognosis. These are the basis of the decision to act in some way or another or of the conclusion that no action is appropriate at that moment. Diagnosis and prognosis are estimates of probability based on relating the patient's condition to knowledge of other patients with similar features.

Because clinicians often call for investigations uncritically, radiologists during the last few years have increasingly emphasised and aimed to impose their role in deciding on the appropriateness of the requested tests and even in the substitution of other tests. Nowadays, radiologists complain if they are asked to carry out a particular test rather than to make a diagnosis using whatever test or tests they judge to be appropriate. This is much healthier than simply responding to diagnostic inflation by the imposition of indiscriminate rationing.

Passing reference at least has to be made to the imminent appearance of inexpensive scanners within the reach of the clinician, the general practitioner and even the layman. It would be prudent now to develop a response to this development, rather than waiting to be surprised. Another dilemma is posed by the use of the live models to demonstrate ultrasonic scanners. Perhaps the possibility of coincidental pregnancy complication or other illness in such circumstances and the consequent threat of opportunistic litigation may be inhibitory.

Hippocrates said, 2400 years ago, "The treatment I adopt shall be for the benefit of my patients, and not for their injury nor for any evil purpose". It is only in the last 300 years or so that doctors have really had to balance harm, or risk, against benefit; and individual patients often need to be involved in judging the values of the harm and the benefit. No one should want to change this. The dilemma which needs to be faced now arises because society can no longer afford, or is judged politically to be unwilling, to provide more resources for health care. When all possible efficiency savings have been made, when all surplus land and property has been sold, one person's heart transplant is at the expense of 75 people's hip replacements, doing eight ultrasound studies means that one computed tomography examination cannot be done, and so on. In the context of this problem, the question of the hypothetical risk of ultrasound is clearly relatively insignificant in deciding on prudent use. If ultrasonic diagnosis causes any harm, it certainly is not obvious. The prudence of using ultrasound in screening programmes is amenable to financial calculation, and if it makes the economists more comfortable, a notional value can be placed on the possible damage due to ultrasound. It is not fair to expect radiologists to make such judgments in the case of individual patients. Perhaps one day the thinking may be done artificially by computers. For the present, however, it is necessary to be prudent, to use skill and good judgment in the use of resources, in determining the qualifications and mix of trained and capable staff and the balance of appropriate equipment in departments of radiology. Rationed in this way, examinations will be chosen for their appropriateness and ultrasound will be used with prudence.

ACKNOWLEDGMENT

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REFERENCES

AMERICAN INSTITUTE OF ULTRASOUND IN MEDICINE, 1984 *Safety Considerations for Diagnostic Ultrasound* (AIUM, Bethesda)

BANTA, D, BEHNEY, C & ANDRULIS, D., 1978. Assessing medical technologies. *Bulletin of the New York Academy of Medicine, 54,* 113–123.

BRERETON, R. J., 1984 Importance of surgical consultation after ultrasonic diagnosis. *British Medical Journal, 289,* 1618–1619

BRITISH INSTITUTE OF RADIOLOGY, 1986 *The Safety of Diagnostic Ultrasound* (BIR, London), in press.

COHEN, B L., 1980 Society's valuation of life saving in radiation protection and other contexts. *Health Physics, 38,* 33–51.

DAY, M. J., 1984. Benefit and detriment in the medical use of radiation. *British Journal of Radiology, 57,* 977–988.

EUROPEAN FEDERATION OF SOCIETIES FOR ULTRASOUND IN MEDICINE AND BIOLOGY, 1984. Watchdog group's evaluation of the safety of ultrasound. *European Medical Ultrasonics, 6,* 5.

FOWKES, F. G. R., DAVIES, E. R., EVANS, K. T., GREEN, G., HARTLEY, G., HUGH, A. E., NOLAN, D. J., POWER, A. L., ROBERTS, C. J. & ROYLANCE, J., 1986. Multicentre trial of four strategies to reduce use of a radiological test. *Lancet, i,* 367–370.

HIBBARD, B. M., ROBERTS, C. J., ELDER, G. H., EVANS, K. T. & LAURENCE, K. M., 1985. Can we afford screening for neural tube defects? The South Wales experience. *British Medical Journal, 290,* 293–295.

INTERNATIONAL COMMISSION ON RADIOLOGICAL PROTECTION, 1983. Cost benefit analysis in the optimisation of radiation protection. *Annals of the IRCP, 10,* No. 2/3.

JENNETT, B., 1984. *High Technology Medicine* (Nuffield Provincial Hospitals Trust, London), pp. 133–134.

KUNDEL, H. L. & HENDEE, W. R., 1985. The perception of radiologic image information. *Investigative Radiology, 20,* 874–877.

MALONEY, T. W. & ROGERS, D. E., 1979. Medical technology—a different view of the contentious debate over costs. *New England Journal of Medicine, 301,* 1413–1419.

MARGULIS, A. R., 1981. Radiologic imaging: changing costs, greater benefits. *American Journal of Roentgenology, 136,* 657–665.

MEDICAL RESEARCH COUNCIL, 1986. *Report on an Ad Hoc Meeting to Discuss the Risks and Benefits of Obstetric Ultrasound* (MRC, London).

MOLD, J. W. & STEIN, H. F., 1986. The cascade effect in the clinical care of patients. *New England Journal of Medicine, 314,* 512–514.

NATIONAL COUNCIL ON RADIATION PROTECTION AND MEASUREMENTS, 1983. *Biological Effects of Ultrasound.* NCRP Report No. 74 (NCRP Publications, Bethesda).

NATIONAL INSTITUTES OF HEALTH, 1984. Diagnostic ultrasound imaging in pregnancy. *Consensus Development Conference Statement, 5,* No. 1.

NATIONAL RADIOLOGICAL PROTECTION BOARD, 1985. *Cost Benefit Analysis in the Optimisation of Radiological Protection.* Draft ASP (NRPB, Chilton).

NEILSON, J. P., 1979. Ultrasonic screening for fetal growth retardation. *Perinatology/Neonatology, 3,* 42–47.

NEILSON, J. P., MUNJANJA, S. P. & WHITFIELD, C. R., 1984. Screening small for dates fetuses: a controlled trial. *British Medical Journal, 289,* 1179–1182.

NYBORG, W. L., 1985. Optimization of exposure conditions for medical ultrasound. *Ultrasound in Medicine and Biology, 11,* 245–260.

ROBERTS, C. J., FARROW, S. C. & CHARNY, M. C., 1985. How much can the NHS afford to spend to save a life or avoid a severe disability? *Lancet, i,* 89–91.

ROYAL COLLEGE OF OBSTETRICIANS AND GYNAECOLOGISTS, 1984. *Report of the RCOG Working Party on Routine Ultrasound Examination in Pregnancy* (RCOG, London).

SANDLER, G., 1979. Costs of unnecessary tests. *British Medical Journal, ii,* 21–24.

SHOWSTACK, J. A., STONE, M. H. & SCHROEDER, S. A., 1985. The role of changing clinical practices in the rising costs of hospital care. *New England Journal of Medicine, 313,* 1201–1207.

ULRICH, W. D., 1971. Ultrasound dosage for experimental use in human beings. In *Report No. 2, Project M 4306 01-1010 BXX9* (Naval Medical Research Institute, Bethesda).

ULRICH, W. D., 1974. Ultrasound dosage for nontherapeutic use on human beings—extrapolations from a literature survey. *IEEE Transactions on Biomedical Engineering, BME-21,* 48–51.

VIRE-OLOGIST, 1986. Pitfalls in clinical budgeting. *Lancet, i,* 568.

WELLS, P. N. T., 1974. The possibility of harmful biological effects in ultrasonic diagnosis. In *Cardiovascular Applications of Ultrasound.* Ed. by R. S. Reneman (North-Holland, Amsterdam), pp. 1–17.

WHITFIELD, C. R. & NEILSON, J. P., 1984. Ultrasonic screening of small for dates fetuses. *British Medical Journal, 289,* 1618.

Correction

Dale, R. G., 1986. The application of the linear-quadratic model to fractionated radiotherapy when there is incomplete normal tissue recovery between fractions, and possible implications for treatments involving multiple fractions per day. *British Journal of Radiology, 59,* 919–927.

Equation (9) in this paper, on page 921, appeared with the expression $(1-K^2)$ as the denominator. $(1-K)^2$ is the correct expression.

Please would readers amend their copies.

Book review

Computed Tomography for Radiographers By M. J Brooker, pp. vii + 121, 1986 (MTP Press Ltd, Lancaster), £24 95.
ISBN 0-85200-920-8

This book is aimed at student radiographers and radiographers studying for the Higher Diploma It is divided into two sections; the first describes technical aspects, and the second clinical aspects of computed tomographic scanning.

In the first section an excellent description is given of the scanner gantry and table, relating equipment design to difficulties in patient handling. This section then discusses X-ray production, photon detection and the four generations of computed tomography (CT) scanners Diagrams are widely used to illustrate these basic principles. Unfortunately, there are some inconsistencies between the diagrams and the text In describing the variations between scanners of different generations, statements are made which, although not incorrect, need to be expanded to avoid confusion to readers with no experience of CT The variation in radiation dose between the different scanners is explained poorly, with incomplete reference to the exposure factors used. A table of radiation doses would have been a great asset.

The remaining chapters in the first section deal with image display and recording, image artefacts and departmental design Apart from some confusion over window width and level, these chapters contain many valid and important points and are well illustrated.

The second part of the book deals mainly with patient preparation and scanning technique, including chapters on radiotherapy planning, interventional techniques and reformatting Once again, much useful information is given, especially in the aspects of patient care, although some sections would have benefited from more detailed descriptions. For example, in describing the use of contrast media no mention is made of the difference between enhancement characteristics of the brain and those of other organs In the discussion on positioning the patient for brain imaging, no reference is made to methods which can be used to reduce radiation dose to the lens of the eye.

Obviously, scanning techniques vary from department to department and it is difficult to be dogmatic about correct scanning methods. Each anatomical area under investigation has been covered and exposure factors quoted. Perhaps the author would have been wise to have omitted these factors, as other users of the same CT systems may argue that they are on the high side. The chapter covering radiotherapy planning and specialised techniques is well presented, with good illustrations and explanations of the various methods.

The final chapters are devoted to anatomy and pathology, the majority of images are CT scans in the transaxial plane. Unfortunately, some of the illustrations in this section are of rather poor quality, with some of the computer annotations being illegible. Also, it seems strange that magnetic resonance images should be included when no reference has been made to this imaging technique in the text.

While there is a definite need for a book of this type, and although some very good points have been made with much useful information, several sections need expansion to avoid confusing those radiographers with no previous experience of CT scanning

C. W HART

1986, *The British Journal of Radiology*, 59, 1153–1158 DECEMBER 1986

Magnetic resonance imaging of the temporo-mandibular joint and meniscus dislocation

By E. Avrahami, *R. Schreiber, *J. Benmair, *Z. Paltiel, *J. Machtey and †I. Horowitz

Departments of Radiology and †Oral Surgery, Tel-Aviv Medical Center and Tel-Aviv University Sackler School of Medicine, and *the Elscint MRI Center, Herzlia, Israel

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ABSTRACT

A preliminary study of the temporo-mandibular joint (TMJ) by magnetic resonance imaging (MRI) was performed. Ten asymptomatic volunteers with no clinical history of TMJ disorder and five patients with a recent history of trauma to the TMJ were examined using a special surface coil. The meniscus, which is only slightly brighter than the surrounding tissue, gave a high signal and was demonstrated very clearly in its normal position in the controls and shown to be dislocated in the post-trauma cases. Four criteria for identification of the temporo-mandibular meniscus were established in the normal cases and compared with the findings in the pathological cases.

The temporo-mandibular joint (TMJ) is the articulation between the mandibular condyle and the glenoid fossa and articular eminence of the temporal bone. An articular disc, the meniscus, divides the articulation into upper and lower compartments. The meniscus is oval in shape and thinner in the middle, giving it a biconcave form. A portion of the lateral pterygoid muscle is inserted into the anterior part of the meniscus, modulating the synchronous movement of the meniscus with the head of the condyle (Manzione et al, 1984a,b,c).

Most patients complaining of TMJ problems are suffering from the dysfunction syndrome. Some cases have an extra-articular cause; others have an internal derangement involving the meniscus (Guralnik et al, 1978; Helms et al, 1983; Manzione et al, 1984b,c).

Considerable effort has been put into finding a reliable, non-invasive imaging technique that will demonstrate clearly the position of the meniscus. Computed tomography (CT), while encouraging, has, so far, had only limited success (North & Rice, 1981).

Magnetic resonance imaging (MRI) seems to provide a clear anatomical picture of the soft tissues of that area and, when used with surface-coil technology, has marked advantages over other imaging techniques. It is non-invasive, does not require ionising radiation, has no known side-effects, and has an excellent correlation with arthrography of the TMJ. The meniscus is demonstrated with the configuration of a biconcave lens having a thick posterior band, a thin central portion and a thick anterior band. If dislocated, the meniscus can be seen displaced anterior to the condylar head, with the jaw in the closed position (Katzberg et al, 1985). The meniscus has a low signal in the T_1 and T_2 images, similar to cortical bone. Perforation of the disc was demonstrated and confirmed by surgery. Magnetic resonance imaging also gave information about fibrous adhesions, ankylosis and post-surgical appearances (Harms et al, 1985).

PATIENTS AND METHODS

A group of 10 asymptomatic volunteers, six men and four women aged 18–38 years, underwent MRI of the right and left temporo-mandibular joints.

Scans were performed on an Elscint GYREX S-5000, a superconducting magnet with 0.5 T field strength, whole-body MRI scanner. A single-turn, circular surface coil, 12 cm in diameter, was used as a transmitter and receiver. Their improved signal-to-noise sensitivity gives surface coils a significant advantage over whole-body or head coils for imaging superficial structures. This advantage decreases with distance from the coil, so that proper coil design is vital for imaging at the proper level. The parameters were: (a) field of view, 12 cm; (b) spatial resolution, 0.47 mm; (c) number of averages, 1; (d) slice thickness, 0.5 mm.

Multislice spin-echo sequences with time to repeat (TR) of 600 ms, 1000 ms, 1200 ms and 1400 ms, and time to echo (TE) of 28 ms and 56 ms were used. Reconstruction was done with the 2DFT technique. A 256 × 256 acquisition matrix was used. Slice width was taken at 5 mm. Imaging was performed with a surface coil located at the area of the TMJ and the examinations were performed in both closed- and open-mouth positions.

After imaging in the axial, coronal and sagittal planes, the sagittal plane was preferred in the demonstration of TMJ anatomy (Figs 1–4), although a change of 2 mm or 3 mm in the sagittal plane can profoundly affect the image of the meniscus.

Five patients, three women and two men aged 19–41 years, with a recent history of trauma to the TMJ and with symptoms suggestive of internal derangement of the meniscus, underwent the same procedure (Figs 5–7). Internal derangement of the meniscus was well documented in the closed-jaw position. In the open-jaw views, after the click, the dislocated meniscus returned

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Author for correspondence: E. Avrahami, M.D., Department of Radiology, Tel-Aviv Medical Center, Ichilov Hospital, 64 239 Tel-Aviv, Israel.

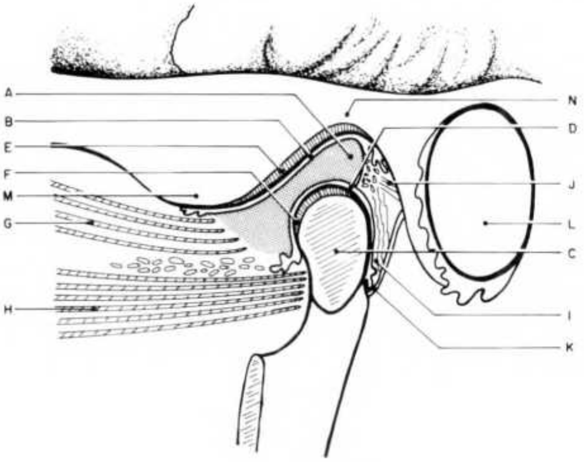

FIG. 1.
Schematic view of the TMJ area: A = meniscus; B = superior cavity; C = condylar head; D = inferior cavity; E = articular surface of the glenoid fossa; F = articular surface of the condylar head; G = external pterygoid muscle, superior belly; H = external pterygoid muscle, inferior belly; J = bilaminar zone, superior stratum; K = posterior part of capsule; L = external auditory meatus; M = articular eminence; N = glenoid fossa.

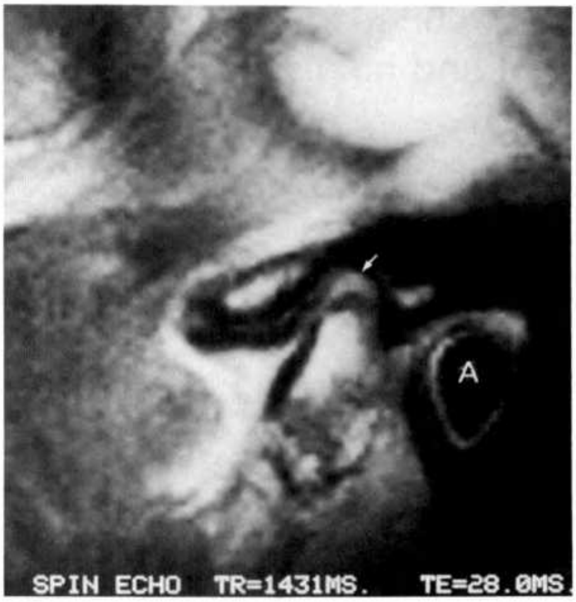

FIG. 2.
Normal left TMJ. The meniscus (arrow) is centrally placed between the condylar head and the articular surface of the glenoid fossa. A = external auditory meatus.

above the head of the mandibular condyle. The MRI findings correlated excellently with the clinical symptoms.

CASE REPORTS

Case 1

A 19-year-old female was referred after sustaining an injury to her chin. Prior to the trauma, there had been no complaint of any pain or malfunction in the TMJ. At the acute stage, pain, swelling and limitation of opening were noted. Two weeks after the trauma, a noisy click appeared at 31 mm opening of the jaw, with limitation and locking of mandibular movements on both sides. A follow-up examination 3 months later revealed two symmetrical palpable condyles, slight tenderness of the masticatory muscles, normal occlusion, and limitation of mandibular movement up to 23 mm of the opening of the jaw. Locking occurred on every trial opening. After a very noisy click and an "S" movement of the mandible, the patient reached a full opening of 40 mm. Conventional radiographs of the TMJ were within normal limits. Coronal CT examination of the TMJ did not demonstrate fractures of the head of the mandibular condyle. The MRI examination demonstrated the meniscus of both temporo-mandibular joints to be dislocated anteriorly to the head of condyle on closed-jaw view. After the click (open jaw), the meniscus returned to its position above the head of the condyle.

Case 2

A 20-year-old male was referred because of pain and locking of the TMJ. Nine months earlier he had been involved in an accident in which he sustained injury to both condylar areas. Prior to the trauma, the patient was completely asymptomatic. During the 9 months after the accident, the patient was treated with analgesics, muscle-relaxing physiotherapy and bite-blocks, but all with limited success. No surgical intervention was performed. On opening of the mouth, a painful and restricted "S" movement up to 34 mm was recorded. On

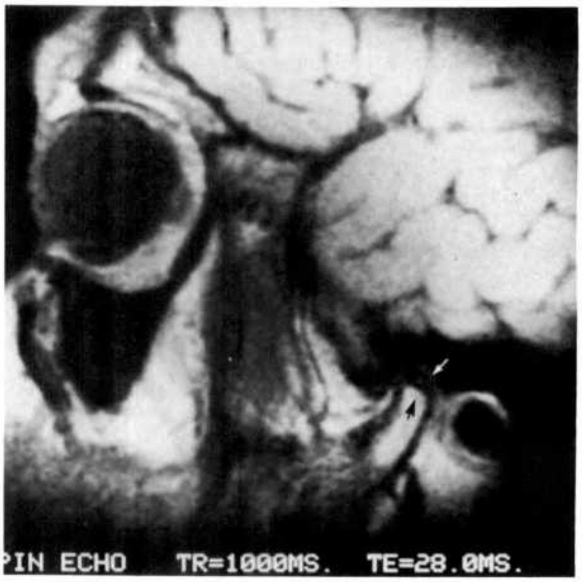

FIG. 3.
Normal left TMJ. Note the distance between the highest part of the bone marrow of the condylar head (arrow) and the articular surface of the glenoid fossa (arrow).

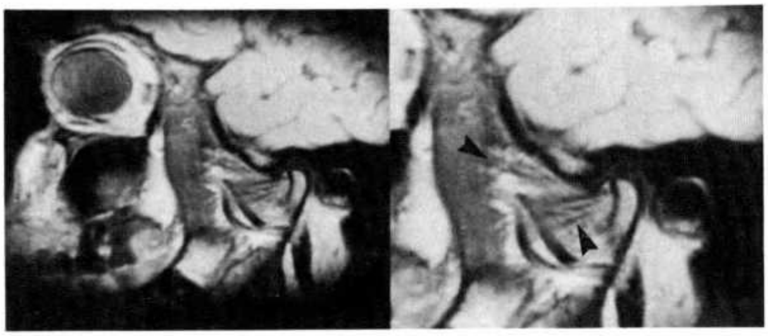

FIG. 4.
Normal left TMJ. The right image is a magnified view of the left slice. Visualisation of the fibres of the superior (upper arrow) and inferior (lower arrow) belly of the external pterygoid muscle. The bone marrow of the condylar head and the articular surface of the glenoid fossa are also well demonstrated.

examination, two symmetrical condyles could be felt and there was tenderness over the left condylar area and masticatory muscles. Occlusion was normal. Conventional radiographs of the temporo-mandibular joints were normal and coronal CT slices of the joints excluded fractures of the head of the mandibular condyle.

Cases 3–5

The remaining three patients had similar features (Table I). They had all experienced a noisy click of one or both temporo-mandibular joints on opening of the mouth, and all were treated conservatively. All had normal conventional radiographs of both joints. Fractures of the head of the mandibular condyle were excluded by coronal CT; MRI demonstrated unilateral or bilateral anterior dislocation of the affected TMJ. These patients had sustained injury to the TMJ areas 2 weeks to 3 months prior to the clinical symptoms, and all had been previously asymptomatic.

RESULTS

A total of 30 temporo-mandibular joints were scanned by MRI in closed- and open-jaw positions. In seven, meniscal dislocation was demonstrated which was reducible in all of the selected patients. No bony changes or adhesions were noted.

The mandibular condyle, glenoid fossa, articular eminence, lateral pterygoid muscles, meniscus, external auditory meatus and maxillary sinus are clearly demonstrated in Figs 1–3. In the group of asymptomatic patients, the following observations were made.

(1) The mandibular condyle, which is seen with high-intensity signal due to its bone marrow content, is centrally located in the glenoid fossa, which can be identified by its very low intensity of signal (dense bone) (Figs 1, 2).

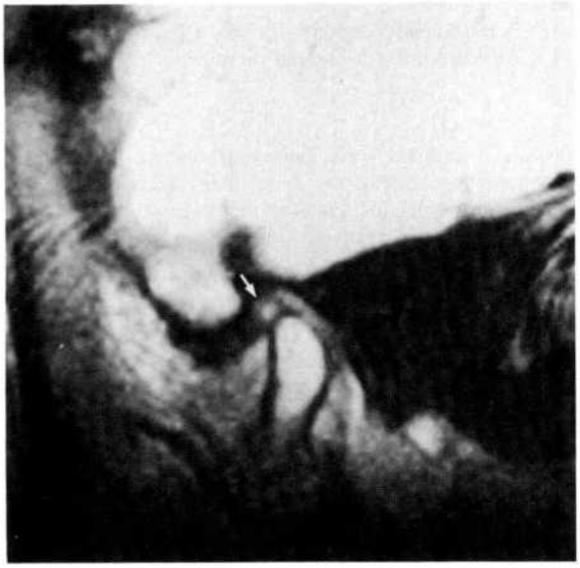

FIG. 5. *Case 1.*
The left meniscus (arrow) is anteriorly located at the condylar head, which is eccentrically located in the glenoid fossa.

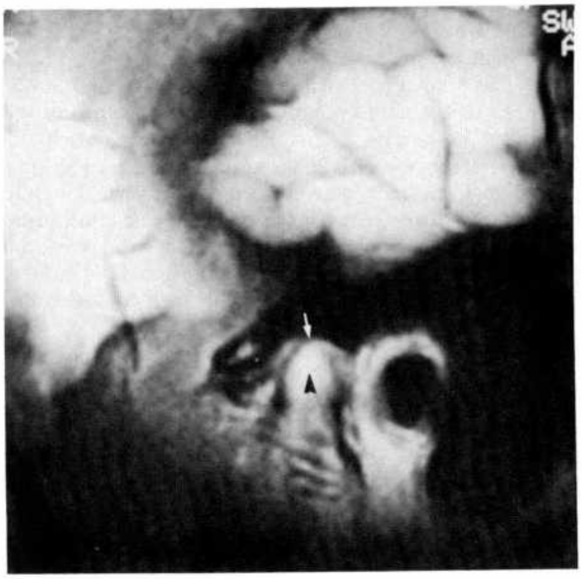

FIG. 6. *Case 1.*
Five millimetres deeper view of the left TMJ showing significant reduction of the distance between the condylar head (lower arrow) and the glenoid fossa (upper arrow).

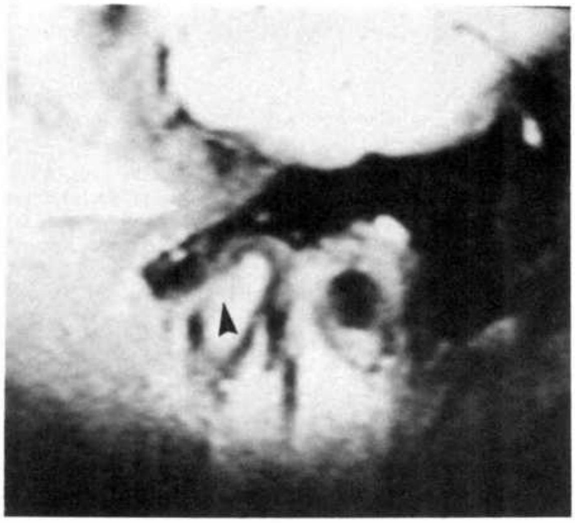

FIG. 7. *Case 2.*
Anterior dislocation of the left meniscus (arrow). Reduction of the distance between the condylar head and the glenoid fossa. The meniscus gives a high signal. In this cut it is of oval shape. It is somewhat darker than the bone marrow of the mandibular condyle. The angulated bright linear structure which represents the superior belly of the external pterygoid muscle is seen more anteriorly.

(2) The intra-articular space between the condyle and the glenoid fossa is clearly delineated. The width of the joint space was assessed and the maximum distance measured between the lowest point of the articular surface of the glenoid fossa and the highest point of the bone marrow of the condylar head (Fig. 3). This was found to be approximately 5 mm.

(3) The central part of the meniscus is located above the head of the mandibular condyle in the depth of the glenoid fossa (Fig. 2). The meniscus itself is demonstrated as a bright structure, limited superiorly by the dark cortex of glenoid fossa and inferiorly by the dark cortex of the mandibular condyle. The connection of the anterior portion of the meniscus with the superior belly of the lateral pterygoid muscle is seen as a higher signal (bright structure), delineated superiorly and inferiorly by lower signals (darker structures), most probably belonging to the meniscus. The most posterior of the meniscal bright structures probably represents fatty tissue of the bilaminar zone, which gives poor demarcation of the most posterior part of the meniscus (Fig. 2).

(4) The fibres of the lateral pterygoid muscle divide into two heads which can be clearly seen inserted into the anatomical neck of the condyle and the anterior part of the meniscus (Fig. 4). They were shown in all cases clearly in a plane 5 mm lateral to the plane where the meniscus had best been demonstrated on TR 1200 ms and TE 28 ms. The coronal and axial images of the meniscus were less clear because of the larger distance to the surface coil. The open-mouth images were less diagnostic and are not considered further.

The following observations were made in the five trauma cases.

Case 1 (Figs 5, 6)

(1) An eccentrically located mandibular condyle (Fig. 5), pushed posteriorly and inwards in relation to the concavity of the glenoid fossa.

(2) The meniscus, which gave a high signal, could be seen anterior to the condyle (Fig. 5) as a bright, round structure. No concavity was demonstrated because of the meniscal rotation.

(3) The intra-articular space was reduced to 1–2 mm (Fig. 6).

Case 2 (Fig. 7)

(1) The mandibular condyle was situated deeply in the glenoid fossa.

(2) A markedly reduced joint space (less than 2 mm).

(3) An anteriorly dislocated meniscus.

Cases 3–5

Similar findings were demonstrated in these three patients: the condyles lay deep in the glenoid fossa or were eccentrically located; the meniscus was dislocated anteriorly and the intra-articular space was reduced to 2 mm or less.

TABLE I

THREE POST-TRAUMATIC PATIENTS WITH ANTERIOR DISLOCATION OF THE MENISCUS, DOCUMENTED BY MRI

Case	Age (years)	Sex	Affected TMJ	Pain, tenderness	Jaw opening by click (mm)	Swelling	Crepitations	Location of condylar head on MRI	Time of clinical diagnosis after trauma
3	31	F	Right	None	31	+	–	Eccentric	4 weeks
4	41	F	Left	Mild	33	–	–	Eccentric	3 months
5	20	M	Both	Moderate	27	+	+	Concentric left, eccentric right	2 weeks

Conclusion

The TMJ in this series was demonstrated normally as a biconcave, bright structure located above the mandibular condyle. When dislocated, the meniscus had a different shape (round or oval) due to its rotation and lay anterior to the condyle at various height levels. On opening the mouth, and after the click, the meniscus returned to its position above the condyle and the MRI appearance was similar to that in normal patients.

Discussion

The central portion of the meniscus is composed of collagen organised in anteriorly–posteriorly orientated sheets. Chondroid cells have not been identified in it below the age of 30 years. The posterior attachments of the meniscus are part of the bilaminar zone, which contain two strata of fibres with connective tissue and fat between them The superior stratum, attached to the tympanic plate, is composed of elastin rather than collagen. Since the meniscus in the healthy TMJ is tightly attached to the medial and lateral aspects of the condyle, its attachment to bone posteriorly must be elastic in order to allow it to move forward with the condyle. The inferior stratum of the bilaminar zone is not stretched as the condyle moves forward because the meniscus also rotates posteriorly, relieving any tension in this stratum Above the postero-superior aspect of the condyle, and anterior to the bilaminar zone, the meniscus is very vascular. This area is called "genu vasculosa" (the vascular knee) Blood vessels completely encircle the avascular central area of the meniscus, with blood being shunted back and forth with jaw function to compensate for changes in volume of the condyle as it vacates one space and fills another. The anterior extension of the meniscus at its attachment to the superior belly of the lateral pterygoid is also very vascular. The higher vascularity and, therefore, higher concentration of hydrogen atoms explain the higher signal of the meniscus, which is demonstrated as a bright structure The superior belly of the lateral pterygoid muscle and the anterior part of the bilaminar zone (because of its fat content) have a hydrogen atom content similar to that of the meniscus and there is, therefore, no clear delineation of the meniscus anteriorly and posteriorly

The demonstration of the meniscus with higher signals as a bright structure correlates with some of the findings of Harms et al (1985). The low signal received from the meniscus and its demonstration as a dark structure (Katzberg et al, 1985) could be explained by different time to echo

Conventional radiographic and CT studies of the TMJ are of great importance in assessing bony abnormalities (Kaban & Bertolani, 1981; Horowitz et al, 1982, Avrahami et al, 1984, Avrahami & Horowitz, 1984; Thompson et al, 1984). However, traumatic degenerative arthritis, ankylosis and neoplasia account for a small percentage of patients with TMJ symptoms. Katzberg et al (1980) showed no significant difference in the condylar position between normal patients and those with an anteriorly displaced meniscus. While TMJ arthrography indirectly visualises the intra-articular anatomy, the morbidity of that invasive technique limits its use. Manzione et al (1983, 1984a,b) have compared CT examination with arthrography of the TMJ with good results.

Using MRI, the ability to demonstrate the meniscus in any desired plane without reconstruction techniques has an obvious advantage over other modalities. An important advantage is the lack of bone artefact and interference, thus allowing the examination of the meniscus itself. Examination with a surface coil significantly improved the visualisation of the TMJ area, creating images comparable with those in anatomical atlases.

We recommend the performance of additional MRI sequences, changing the depth of the sagittal plane by 2–3 mm to obtain optimal imaging of the meniscus.

The first 10 patients examined were assumed to represent normal anatomy, since no history or clinical findings of TMJ disturbances was forthcoming.

The five cases representing disease of the TMJ were selected from a large group of symptomatic patients suffering from TMJ dysfunction syndrome. The fact that these 10 symptomatic patients presented a very clear normal history before injury and a clear clinical picture of an intracapsular disease (probably internal derangement) after injury justified the comparison between the two groups.

The MRI findings in symptomatic patients with sagittal images in the closed-mouth position are: deep and eccentric position of the condyles, reduction of joint space, and anterior position of the meniscus. These findings are sufficient to establish the diagnosis of anterior dislocation.

The advantage of the method is that it is non-invasive and demonstrates the soft tissues effectively without morbidity or irradiation

REFERENCES

Avrahami, E & Horowitz, J, 1984 Chip fractures of the mandibular condyle. *Head and Neck Surgery, 6*, 978–981

Avrahami, E., Horowitz, J & Cohn, D F, 1984 Computed tomography of the temporo-mandibular joint *Computerized Radiology, 8*, 211–216

Guralnik, W, Kaban, L B & Merril, R. G, 1978. Temporo-mandibular joint afflictions *New England Journal of Medicine, 299*, 123–129.

Harms, S E., Wilk, R. M., Wolford, L. M, Chiles, D G & Milam, S. B., 1985. The temporomandibular joint Magnetic resonance imaging using surface coils *Radiology, 157*, 133–136.

Helms, C. A., Katzberg, R W, Morrish, R & Dolwick, M F, 1983 Computed tomography of the temporo-mandibular joint *Journal of Oral and Maxillofacial Surgery, 41*, 512–517.

Horowitz, J, Avrahami, E & Mintz, S S, 1982 Demonstration of condylar fractures of the mandible by computed tomography. *Oral Surgery, Oral Medicine, Oral Pathology, 54*, 263–268

Kaban, L. B & Bertolani, C. N., 1981. The role of the CT scan in the diagnosis of TMJ ankylosis. *Journal of Oral Surgery, 39,* 370–372.

Katzberg, R W., Dolwick, M. F, Helms, C. A, Hopens, T., Bales, D. J & Goggs, G. C., 1980. Arthrotomography of the temporo-mandibular joint. *American Journal of Roentgenology, 134,* 995–1003

Katzberg, R. W., Schenk, J., Roberts, D., Tallents, R. H., Manzione, J. V., Hart, H. R., Foster, T. H, Wayne, W S. & Bessette, R. W., 1985. Magnetic resonance imaging of the temporomandibular joint meniscus. *Oral Surgery, Oral Medicine, Oral Pathology, 59,* 332–335.

Manzione, J. V, Katzberg, R. W. & Manzione, T. J., 1984a. Internal derangement of the temporo-mandibular joint. I Normal anatomy, physiology and pathophysiology. *International Journal of Peridontics and Restorative Dentistry, 4,* 9–16.

Manzione, J. V., Katzberg, R W. & Manzione, T. J., 1984b. Internal derangements of the temporo-mandibular joint. II Diagnosis by arthrography and computed tomography. *International Journal of Peridontics and Restorative Dentistry, 4,* 17–27.

Manzione, J. V., Katzberg, R. W., Brodsby, G. L., Seltzer, S. E. & Mellins, H. Z., 1984c. Internal derangements of the temporo-mandibular joint. Diagnosis by direct sagittal computed tomography. *Radiology, 150,* 111–115. .

Manzione, J. V., Seltzer, S. E., Katzberg, R. W., Hammerschlag, B. & Brian, F., 1983 Direct sagittal computed tomography of the temporo-mandibular joint. *American Journal of Roentgenology, 140,* 165–167.

North, A. F. & Rice, J., 1981. Computed tomography in oral and maxillofacial surgery. *Journal of Oral Surgery, 35,* 199–207.

Thompson, J. R., Christiansen, E., Hasso, N. & Hinshaw Jr, D. B., 1984. Temporo-mandibular joints. High resolution computed tomographic evaluation. *Radiology, 150,* 105–110.

1986, *The British Journal of Radiology*, 59, 1159–1162 DECEMBER 1986

Screen–film mammography versus xeromammography in the detection of breast cancer*

By J. T. Cuttino Jr, M.D., B. C. Yankaskas, Ph.D. and †E. O. L. Hoskins, M.B., F.R.C.R., F.R.C.P. Ed.

Department of Radiology, University of North Carolina School of Medicine, Chapel Hill, North Carolina 27514, USA and †Department of Radiology, Guy's Hospital, London

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ABSTRACT

There are two common methods of obtaining high-quality screening mammography: screen–film mammography (more simply, mammography) using a dedicated unit, and xeromammography. We studied the accuracy of the two techniques in detecting breast cancer by a retrospective study, analysing accuracy of interpretation in cases where both mammography and xeromammography were performed. Seventy-six patients were considered with 86 biopsies and mammograms resulting in detection of 32 cancers and 54 benign lesions. There was no difference in accuracy of interpretation between mammography and xeromammography. The sensitivities were: mammography 0.91, xeromammography 0.88. The specificities were: mammography 0.63, xeromammography 0.75. We conclude that both modalities are comparable in detecting cancer when optimal technique and experienced personnel are used.

Breast cancer is the most frequent cancer and the leading cause of death in women, affecting one out of every 11 American women (Seidman, 1972). Accurate and early detection are essential in controlling this disease. Mammography is accepted as a significant advance in the early detection of breast cancer (McLelland, 1978; Anderson et al, 1979; Dodd, 1984; Moskowitz, 1984).

With the renewed emphasis on screening mammography and breast-imaging centres, the use of mammography is increasing. The practice of the best possible mammography requires optimal technique and an experienced, knowledgeable interpreter. There are two well established techniques used in mammography screening: screen–film mammography using a dedicated unit with low-kilovoltage X-ray source (molybdenum) and screen–film systems, and xeromammography.

There are many factors to consider in deciding which mammographic system to employ: cost, radiation dose, ease of use, durability, reliability, personal preference, and accuracy of the technique. Accuracy of cancer detection is obviously the main consideration and any other factor would be secondary if one technique were more accurate than the other.

At the time of this study at Guy's Hospital in London, both mammography and xeromammography were being performed routinely on each patient. This enabled us to undertake a retrospective study of the accuracy of the two techniques in detecting breast cancer.

PATIENTS AND METHODS

All patients having a breast biopsy performed at Guy's Hospital Breast Unit from 1978 to 1980 were identified. The medical records of these patients were reviewed for identification of their mammograms, descriptive information, and pathological and surgical results.

A Philips-Mammo D unit with molybdenum target tube, 30 μm Mo filter and nominal focal spot size 0.6 mm was used with Kodak Min-R screens and Kodak Min-R film. No grids were used. Films were processed in a Pako XU 2 min processor at 30°C. Average exposure settings used were 28–35 kVp and automatic mAs exposures. The xeromammography technique utilised the same Philips Mammo D unit (same tube and filtration) with exposure settings of 45–49 kVp, 200 mA and 0.08–1.0 s. Dosimetry studies using lithium fluoride chips were performed in 12 patients. For mammographic studies one thermoluminescent dosemeter (TLD) was placed on each breast in the upper medial quadrant and left in position for all four radiographs. For xeromammographic studies a separate TLD was left in a similar position for the two views. Xeroplates (positive mode) were processed with a Xerox 125 unit.

Dosimetry measurements using lithium fluoride chips gave mean skin entrance doses of 1.32 ± 0.44 R ($3.41 \times 10^{-4} \pm 1.14 \times 10^{-4}$ C/kg) (combined four views) for mammograms ($n = 12$) and 6.87 ± 1.38 R ($17.72 \times 10^{-4} \pm 3.56 \times 10^{-4}$ C/kg) (combined two views) for xeromammograms ($n = 12$).

Mammographic examination at Guy's consists of cranio-caudad and medio-lateral views with screen–film combinations and a Lundgren-type oblique medio-lateral survey view by xeromammography (Lundgren, 1979). For purposes of comparison medio-lateral views were used in both techniques. The mammograms were read in random order by one of us

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Reprint requests to Dr J. T. Cuttino Jr.

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(J.C.), without knowledge of the pathological result, and each was rated as having evidence of cancer, possibly having evidence of cancer, or having no evidence of cancer. The reader is experienced in mammography and in interpreting both types of radiograph. The xeromammograms were read in the same manner at least 2 weeks after the mammogram readings, to reduce the likelihood of recall of previous interpretation. At the time of reading, note was made of the presence and character of microcalcifications and a hand-held magnifying lens was used throughout. The interpretations from the two readings (mammographic and xeromammographic) were compared with the pathological results and analysis made of the sensitivity, specificity and predictive value for the separate readings. Differences between the sensitivity and specificity values were calculated using a test for difference in correlated data (Galen & Gambino, 1975). In addition, the techniques were compared as to agreement of results, using a kappa statistic (Fleiss, 1981).

Results

A review of medical records identified 76 patients who had had 86 biopsies and associated mammograms. The mean age of the patients was 51.5 (range 27–75) years. Of the 76 patients, 32 had biopsies positive for cancer and 54 had benign disease.

The results of the accuracy analysis are presented in Table I. For determining sensitivity and specificity we have chosen to err on the side of false positives by calling indeterminate mammographic interpretations positive.

The sensitivity of mammography was 0.91, and of xeromammography, 0.88. There was no statistical difference between the two ($t = 0.29$, $p > 0.8$). The specificity of mammography was 0.63; of xeromammography, 0.75. There was no statistical difference between mammography and xeromammography in specificity ($t = 1.8$, $p > 0.05$).

Given that the two methods do not give different results, the next questions addressed were: how strong is the agreement between mammography and xeromammography? Also, when there is disagreement, which is more accurate? Table II shows the results of the agreement analysis. Kappa statistic for agreement equalled 0.67, with a standard error of 0.11. Kappa is 0 when agreement is expected exactly by chance, and 1 when there is complete agreement. A kappa of 0.67 shows good agreement between mammographic and xeromammographic interpretation.

TABLE I

Accuracy of mammography and xeromammography with 95% confidence intervals

	Mammography	Xeromammography
Sensitivity	0.91 ± 0.06	0.88 ± 0.06
Specificity	0.63 ± 0.10	0.75 ± 0.10
Positive predictive value	0.58 ± 0.10	0.67 ± 0.10
Negative predictive value	0.92 ± 0.06	0.91 ± 0.06

TABLE II

Matched-pair agreement of each mammogram and correlated xeromammogram

Mammography results	Xeromammography results		
	Cancer	No cancer	Total
Cancer	39	11	50
No cancer	3	33	36
Total	42	44	86

The pathology results for the patients compared with the overall mammographic and xeromammographic interpretations are shown in Table III. In the three patients with cancer, the mammographic interpretation was correctly interpreted twice and the xeromammographic once. In the 11 patients without cancer, the mammogram was correctly interpreted twice and the xeromammogram nine times (Table IV). Overall, when there was disagreement between the two interpretations, the reading from the mammogram was accurate 29% of the time, and from the xeromammogram, 71% of the time.

Characterisation of calcifications did not differ between the mammogram and the xeromammogram. In

TABLE III

Comparison of radiographic results with pathology for mammography and xeromammography

Technique	Interpretation	Pathology results	
		Cancer	Benign
Mammography	positive	29	21
	negative	3	33
Xeromammography	positive	28	14
	negative	4	40

TABLE IV

Comparison of radiographic and pathological results in cases where mammographic and xeromammographic results differed

	Pathology results	
	Cancer	No cancer
Mammogram +/xeromammogram −	2	9
Mammogram −/xeromammogram +	1	2

some instances calcifications were more easily seen with one modality compared with the other, but in no instance was calcification seen with one technique and not the other.

DISCUSSION

Guy's Hospital is a large referral hospital and the cases were referred because of suspicion of disease. However, there were some in which mammography detected the lesion and biopsy was recommended solely on the basis of the mammograms. Case histories were incomplete in some instances and an accurate determination of symptomatic versus asymptomatic individuals was not possible.

Mammography is a well established technique in the early detection of breast cancer (Moskowitz, 1984) It is recognised that optimal technique and experienced personnel are required for the best results Previous studies which have compared accuracy of the detection of breast cancer with mammography and xeromammography have reported superiority of xeromammography (Ruzicka et al, 1965; Wolfe et al, 1971; Brebner & Judelman, 1975). These studies, however, were undertaken before recent significant technical improvements in film–screen technique, *e.g.* molybdenum target anodes and faster, higher-detail film–screen combinations. Indeed, in one of these reports (Brebner & Judelman, 1975) the study was abandoned due to the finding of "increased information and detail" with the xeroradiographic system. Later studies (Egan et al, 1977, Sickles, 1981) showed no major superiority of one technique over the other and even a slight preference for mammography (Egan et al, 1977). In this series, therefore, we have used improved screen–film mammographic and xerographic systems to see if one technique is superior in detecting cancer, and compared them to evaluate specific agreement.

Our dosimetry data show excessively high doses when utilising xeromammography. This is in part due to the molybdenum filtration employed. A shift to aluminium filtration would have reduced the dosage but could not be added as a removable feature on a relatively old unit.

The results of sensitivity, specificity and predictive values found no statistical difference between mammography and xeroradiography.

The high sensitivity (few false negatives) and low specificity (high false positives) can be partially explained by the nature of our analysis. We equated the equivocal result as positive, thus artificially inflating the positive rate from a more realistic clinical situation. Another potential bias of our results is due to the fact that all cases came to biopsy, creating a high prevalence of cancer in the population studied, and reducing the number of disease-free individuals. This would have the effect, statistically, of increasing the predictive value of a positive result, or reducing false positives. This is balanced in our study by the decision to call equivocal studies positive, which would increase the false positives. When comparing the two modalities, both were operating under the same potential bias. Thus, the comparison would not be biased, though the actual values of the sensitivities may not be universally applicable.

The same equipment was used for both mammography and xeromammography, potentially removing the advantage of xeromammography in allowing better imaging of the chest wall. It is possible that the addition of a view that images the chest wall would lower the false negative results since lesions are sometimes detected only on this view (Bassett et al, 1980; Pagani et al, 1980).

Analysis of disagreement data (Tables III and IV) showed that, though not statistically different, there were fewer false positives with xeromammography There was no difference in false negatives Thus, with equal ability to identify positives, xeromammography was slightly better at correctly identifying negatives. Most mammographers and clinicians agree that, in screening, it is most important to reduce the number of false negative examinations. Such a patient is easily lost to follow-up or followed up too late to cure the disease Thus, it is desirable to be conservative and to err on the side of reducing the number of false negatives. False positives, though not desirable because they may lead to needless biopsy, are more acceptable if they result in detection of minimal breast cancer and possible cure of the patient. In this series, we found film–screen mammography and xeromammography equally effective in cancer detection.

Sickles (1982) has shown that xeromammography is better than mammography in detecting microcalcifications in *in-vitro* experimental studies. Our study does not show this in the clinical setting when one pays meticulous attention to detail. Indeed we had cases where calcifications were better shown by xeromammography and cases where the reverse was true. In no case, however, were the calcifications "invisible" We would agree, as a general rule, that they are easier to see with xeromammography (no magnifying lens required) Focal spot size is probably a more important factor than the film receptor in detecting calcifications.

Our results would have been stronger if we had had more than one reader, and a more representative sample of the screened population However, in women referred for biopsy, our results suggest that film–screen mammography and xeromammography are both excellent methods of detecting breast cancer

More recent improvements, including the use of grids for enhanced contrast, are now standard (Egan et al, 1983). The xerography technique has also benefited from the use of aluminium filtration with the negative mode and has the great advantage of being compatible with a tungsten anode. Significant dose reductions have been achieved (Keddy & Brebner, 1980) and other developments, such as magnification, have been instituted since the beginning of our study. It would be speculative to try to anticipate the future method of choice and further studies of this type will be required.

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REFERENCES

ANDERSON, I., ANDREN, L., HILDELL, J, LINELL, F, LJUNGQVIST, U. & PETTERSSON, H, 1979 Breast cancer screening with mammography *Radiology, 132,* 273–276

BASSETT, L W, PAGANI, J. J. & GOLD, R. H., 1980. Pitfalls in mammography: demonstrating the deep lesions. *Radiology, 136,* 641–645.

BREBNER, D. M & JUDELMAN, E., 1975. Comparison of xeromammography and film mammography in the diagnosis of breast lesions. *African Medical Journal, 49,* 1380–1382

DODD, G. D, 1984. Mammography. state of the art *Cancer, 53,* 652–657

EGAN, R. L., GOLDSTEIN, G. T. & MCSWEENEY, M. M., 1977 Conventional mammography, physical examination, thermography and xeroradiography in the detection of breast cancer. *Cancer, 39,* 1984–1992.

EGAN, R. L., MCSWEENEY, M. B. & SPRAWLS, P, 1983. Grids in mammography. *Radiology, 146,* 359–362.

FLEISS, J L., 1981. *Statistical Methods for Rates and Proportions,* 2nd edit (John Wiley and Sons, New York), Chap 11.

GALEN, R. S & GAMBINO, S R., 1975. *Beyond Normality. The Predictive Value and Efficiency of Medical Diagnoses* (John Wiley and Sons, New York)

KEDDY, R J. & BREBNER, D. M., 1980. Negative development xeroradiography of the breast: doses and clinical indications. *British Journal of Radiology, 53,* 325–330

LUNDGREN, B, 1979 Population screening for breast cancer by single view mammography. *Journal of the National Cancer Institute, 62,* 1373–1379

MCLELLAND, R., 1978 Mammography in the detection, diagnosis and management of carcinoma of the breast. *Surgery, Gynecology and Obstetrics, 146,* 735–740.

MOSKOWITZ, M, 1984. Mammography to screen asymptomatic women for breast cancer. *American Journal of Roentgenology, 143,* 457–459.

PAGANI, J. J., BASSETT, L. W, GOLD, R H., BENEDETTI, J, ARNDT, R D, LINSMAN, J. & SCANLAN, R. L., 1980. Efficacy of combined film–screen/xeromammography: preliminary report. *American Journal of Roentgenology, 135,* 141–146

RUZICKA, F. F., KAUFMAN, L., SHAPIRO, G., PEREZ, J. V. & GROSSI, C. E., 1965 Xeromammography and film mammography. *Radiology, 85,* 260–269.

SEIDMAN, H., 1972. *Cancer of the Breast Statistical and Epidemiological Data* (American Cancer Society, New York).

SICKLES, E. A, 1981 Xeromammography versus screen–film mammography. Pros and cons of the two techniques. *Western Journal of Medicine, 134,* 273–274.

SICKLES, E A, 1982. Mammographic detectability of breast microcalcifications *American Journal of Roentgenology, 139,* 913–918.

WOLFE, J. N., DOOLEY, R P & HARKINS, L. E, 1971. Xeroradiography of the breast: a comparative study with conventional film mammography *Cancer, 28,* 1569–1574.

1986, *The British Journal of Radiology*, 59, 1163–1166 DECEMBER 1986

Failure to visualise the abdominal portion of the inferior vena cava with computed tomography: a clue to underlying abdominal pathology

By *John H. Stanley, M.D., †Frank Sanchez, M.D., Ivan Vujic, M.D. and Stephen I. Schabel, M.D.

Department of Radiology, Medical University of South Carolina, 171 Ashley Avenue, Charleston, SC 29425 and †Department of Radiology, Emory University School of Medicine, 1364 Clifton Road NE, Atlanta, Georgia 30322, USA

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ABSTRACT

Failure to visualise the intra-abdominal portion of the inferior vena cava (IVC) using contrast-enhanced computed tomography (CT) is unusual. A review of 1272 contrast-enhanced abdominal CT examinations revealed that the IVC was not visible at one or more levels in only 132 (10.4%). In 57 (43%), non-visualisation was due to pathological processes, most frequently metastatic carcinoma, causing compression or thrombosis of the IVC. In the remainder, technical factors or artefacts could explain the non-visualisation. Techniques and procedures to improve visualisation of the IVC are discussed. Failure to visualise the IVC on CT at any level unexplained by artefacts is abnormal.

Computed tomography (CT) has proved to be an excellent non-invasive method for investigating the inferior vena cava (IVC). Congenital anomalies (Mayo et al, 1983), IVC obliteration, or involvement with primary and secondary neoplasms (Marks et al, 1978; Weyman et al, 1980, Chauhan et al, 1981), as well as caval thrombosis have been described (Zerhouni et al, 1980; Vujic et al, 1981). The abdominal portion of the normal IVC can usually be recognised at all levels below the liver on contrast-enhanced abdominal scans. Failure to visualise the IVC should be considered suspicious and an explanation sought. This study was undertaken to determine the frequency and causes of non-visualisation of the IVC.

METHODS

A review of 1272 consecutive abdominal contrast-enhanced CT scans performed over a 2-year period (January 1981–January 1983) on a GE 8800 CT scanner (scan times 4.8–9.6 s) was undertaken to determine the incidence of failure to visualise adequately any portion of the abdominal IVC. Contiguous slices 1 cm-thick were obtained from the dome of the diaphragm to the symphysis pubis following intravenous contrast enhancement (300 ml of 30% Conray (May & Baker) injected as a rapid infusion through the antecubital vein). In cases where IVC abnormalities were suspected, confirmation by the clinical data, pathological material obtained at surgery or autopsy, standard inferior

TABLE I
NON-VISUALISATION OF ABNORMAL IVC ON CT

Pathological process	No. of patients	IVC segment involved			Totals
		Supra	Renal	Infra	
Carcinoma, cervix	5	—	3	5	8
Carcinoma, prostate	5	2	4	5	11
Renal-cell carcinoma	8	1	8	1	10
Recurrent renal-cell carcinoma	4	2	1	1	4
Lymphoma	5	—	5	4	9
Thrombosis	3	—	—	3	3
Adenocarcinoma (unknown source)	2	—	2	2	4
Abscess (bacterial)	3	2	1	—	3
Left cava	2	—	—	2	2
Trauma	2	—	1	1	2
Carcinoma, pancreas	2	1	1	0	2
Others (see Results)	16	4	10	12	26
Totals	57	12	36	36	84

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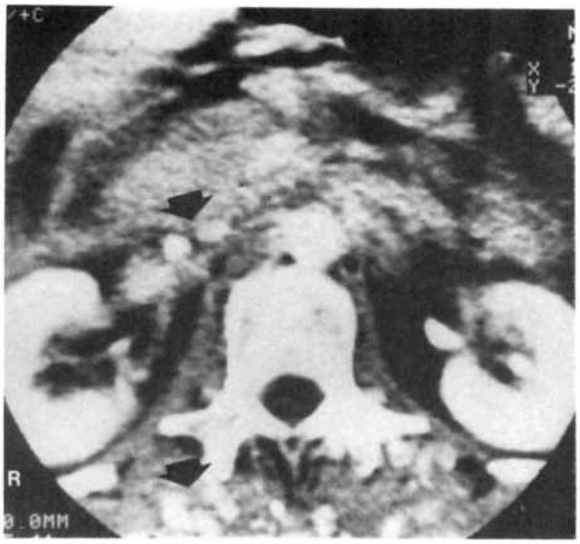
*Author for correspondence and reprint requests.



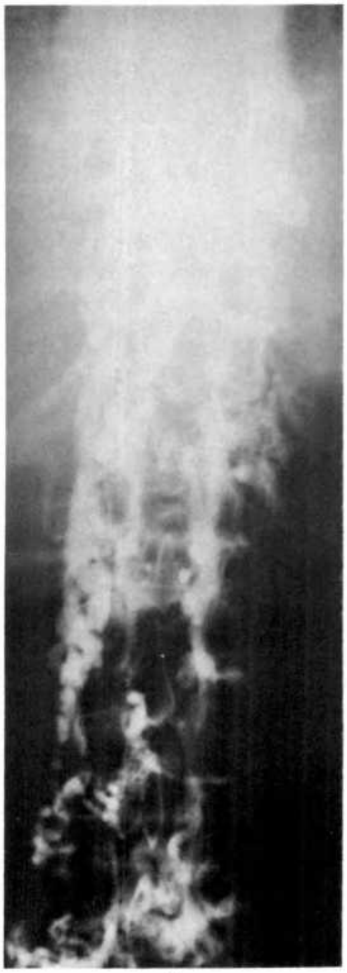


FIG. 1.
(A) There was failure to visualise a normal abdominal IVC in this Egyptian patient with Budd–Chiari syndrome secondary to a previous infection with schistosomiasis. A CT scan during injection of contrast medium into the foot veins demonstrated only collateral vessels (arrows). (B) A standard venocavogram showing numerous paravertebral collaterals without visualisation of the normal IVC.

venocavograms performed via percutaneous femoral vein catheterisation, or CT cavography with contrast-medium injection via the foot veins was obtained. There was a minimum of 18 months of clinical follow-up of these patients.

The IVC was divided into three segments: the suprarenal segment was defined as the area from the entrance of the IVC into the caudate lobe of the liver to approximately 1 cm above the level of the renal veins; the renal segment was 1 cm above and below the entrance of the renal veins into the IVC; and the infrarenal segment was from a level 1 cm below the renal veins to the confluence of the iliac veins. Each CT slice was examined for visualisation of the IVC. Non-visualisation was defined as failure to identify the IVC at any level due to partial or complete loss of the caval margins (*e.g.* adjacent mass effect, or tumour replacement) or the complete absence (*e.g.* congenital absence or chronic thrombosis). The causes for non-visualisation were divided into technical and pathological categories.

RESULTS

Of the 1272 examinations performed, there was failure to visualise part of the abdominal IVC in 132 patients (10.4%). Over half of these (76/132, 58%) were due to technical factors. This most commonly occurred as a result of high-density streak artefact caused by adjacent barium within the gastrointestinal tract or by surgical clips (36/76, 47%). Other frequent technical factors included patient movement (19/76, 38%), a combination of movement and high-density artefacts (15/76, 20%), and inadequate retroperitoneal fat (6/76, 8%).

Approximately one in 20 patients examined (57/1270, 4.5%), slightly less than half of those with non-visualisation of the IVC, had pathological processes producing caval non-visualisation (Figs 1–3). There were 84 segments of the IVC which were not visualised in the 57 patients (Table I). The renal and infrarenal segments were visualised least frequently (36 patients each).

Pathological processes which occurred only once are grouped under "Others" in Table I. These included neuroblastoma, hepatoma, Budd–Chiari syndrome secondary to schistosomiasis, adrenal carcinoma, idiopathic renal vein thrombosis, biliary cystadenoma, tuberculous abscess, phaeochromocytoma, retroperitoneal sarcoma, ovarian dermoid, previous caval ligation, pancreatic pseudocyst, retroperitoneal haemangioma, and metastatic carcinoma of the breast, colon and bladder.

DISCUSSION

Computed tomography offers a quick and accurate non-invasive method of investigating patients with suspected caval abnormalities (Marks et al, 1978; Weyman et al, 1980; Zerhouni et al, 1980; Chauhan et

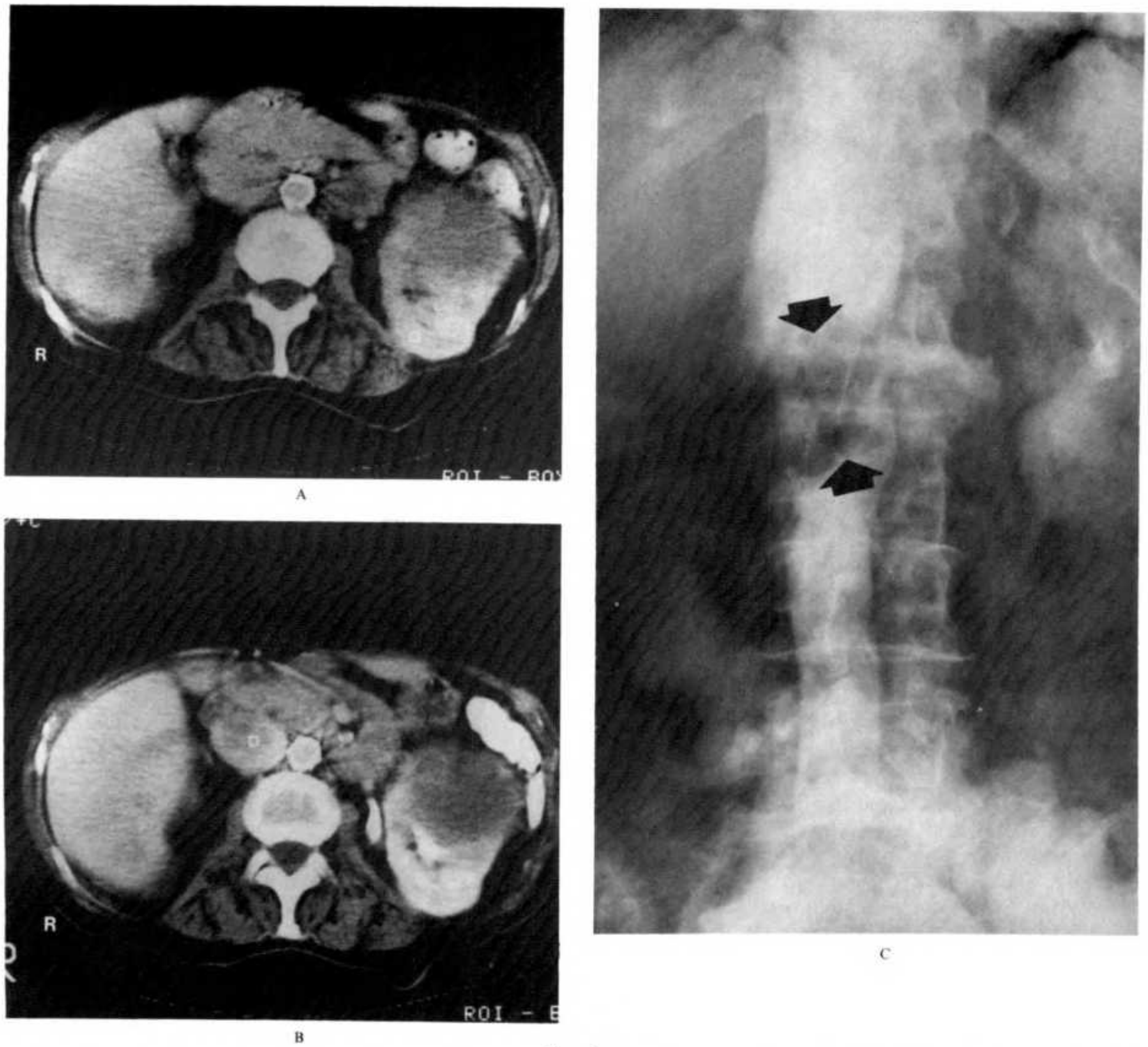


FIG. 2.

(A) The normal IVC was not visualised at the renal or suprarenal level in this patient with bilateral renal-cell carcinoma. (B) A CT scan performed during contrast-medium injection into a foot vein demonstrated almost complete occlusion of the IVC with tumour (cursor on tumour). (C) Standard venocavogram confirmed the CT finding of tumour within the IVC (arrows).

al, 1981; Vujic et al, 1981; Mayo et al, 1983). The IVC is the largest vein in the body and should be easily seen on contrast-enhanced CT scans. Its size, shape and contour should be studied for signs of abnormality on each image of an abdominal CT scan. The only exception to this is the hepatic segment of the IVC which is often difficult to evaluate if the CT examination is performed after the equilibration of intravascular and hepatic parenchymal contrast medium. However, even this segment may be adequately examined using intravenous bolus injections of contrast medium. Since bolus injections were not routinely given to all patients, the area was excluded in this study.

In our series, non-visualisation of the IVC occurred usually as a result of technical causes. Primary or secondary malignancy compressing or directly involving the cava accounted for the majority of the remainder (42/57, 74%). Surrounding lymphadenopathy resulting in loss of fascial planes between the nodal mass and IVC accounted for approximately half (20/42, 48%) the cases of non-visualisation due to malignancy. Surprisingly, the process that most extensively involved the abdominal IVC, producing the longest segments of non-visualisation, was lymphadenopathy due to metastatic carcinoma of the prostrate.

In addition to technical causes and non-visualisation due to masses, absence of the IVC can also account for failure of identification. This is rare, occurring in only

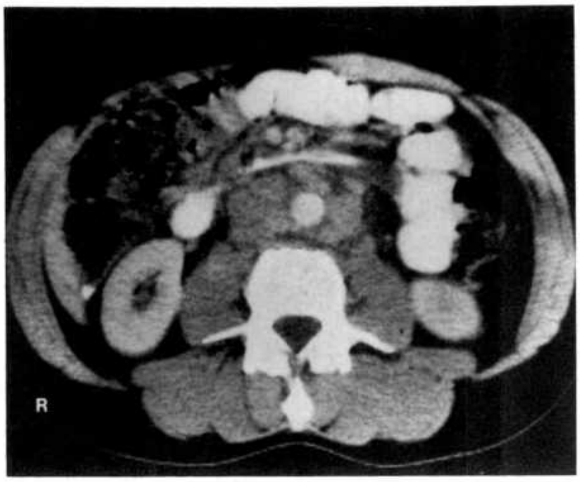


FIG. 3.
In this patient with carcinoma of the prostate, there was diffuse para-aortic adenopathy causing non-visualisation of the renal and infrarenal segments of the IVC.

four cases (0.3%) in this series. In two cases, the IVC was not visible on CT and only small collateral vessels were present on standard cavograms. Each patient had had prolonged periods of bed rest and recurrent venous thrombosis over many years. A third patient with severe atherosclerotic disease had occlusion of the lower abdominal aorta and absence of the infrarenal IVC. The fourth patient was assumed to have congenital absence of the IVC as he had no identifiable IVC and only retroperitoneal collateral veins, with no historical incident to explain caval thrombosis.

While this study did not attempt to determine the presence or absence of IVC obstruction, it is apparent that many conditions known to cause obstruction can also cause non-visualisation. Obstruction of the IVC is usually due to thrombosis, or compression or direct caval invasion by neoplasms (Harris, 1976). The infrarenal segment of the IVC is most commonly obstructed secondary to ascending thrombus formation due to thrombophlebitis and occasionally due to compression by adjacent tumours. Caval thrombosis secondary to ascending thrombophlebitis was an uncommon cause of caval non-visualisation since the thrombosed cava is clearly visualised in the majority of cases. The renal segment of the cava is most frequently obstructed due to direct tumour involvement from renal-cell carcinoma or retroperitoneal spread of other malignancies which were common causes for non-visualisation of the renal segment of the IVC in our series. Obstruction of the suprarenal and hepatic portions of the IVC usually occurs due to primary or secondary liver malignancies.

Twenty-three of 57 patients (40%) with pathological non-visualisation had clinical symptoms (principally, marked lower-extremity oedema) consistent with IVC obstruction. Fourteen of these patients had standard IVC cavograms via femoral vein catheterisation and/or CT cavography performed via foot vein injections. All 14 had IVC obstruction. Eight patients had both CT and standard cavograms and all patients with a positive CT cavogram had a positive standard inferior vena cavogram. Despite anticipating false positive CT examinations performed via foot vein injections (Glazer et al, 1981), we did not encounter this. In the remaining 32 patients with non-visualisation on CT and no clinical evidence of IVC thrombosis, seven with diffuse metastatic disease subsequently developed clinical symptoms consistent with IVC obstruction over the 18-month follow-up period.

In summary, when failure to visualise the abdominal portion of the IVC at any level on a contrast-enhanced CT scan has no technical cause, serious intra-abdominal pathology should be suspected, of which the principal causes are lymphadenopathy secondary to metastatic tumours or direct involvement of the IVC from malignancy. If clinical symptoms of IVC thrombosis are present, almost all patients will have IVC thrombosis or obstruction. This can be confirmed by CT cavography or standard inferior vena cavography.

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REFERENCES

CHAUHAN, M. A., SMITH, P. L., FERRIS, E. J., MURPHY, K., WESTBROOK, K. & SLAYDEN, J. E., 1981. Leiomyosarcoma of the inferior vena cava: angiographic and computed tomography findings. *Cardiovascular and Interventional Radiology*, *4*, 209–214.

GLAZER, G. M., CALLEN, P. W. & PARKER, J. J., 1981. CT diagnosis of tumor thrombus in the inferior vena cava: avoiding the false positive diagnosis. *American Journal of Roentgenology*, *137*, 1265.

HARRIS, R. D., 1976. The etiology of inferior vena cava obstruction and compression. *CRC Critical Reviews in Clinical Radiology & Nuclear Medicine*, *8*, 57–86.

MARKS, W., KOROBKIN, M., CALLEN, V. W. & KAISER, J., 1978. CT diagnosis of tumor thrombosis of the renal vein and inferior vena cava. *American Journal of Roentgenology*, *131*, 843–846.

MAYO, J., GRAY, R., ST LOUIS, E., GROSSMANN, H., MCLOUGHLIN, M. & WISE, D., 1983. Anomalies of the inferior vena cava. *American Journal of Roentgenology*, *140*, 339–345.

VUJIC, I., STANLEY, J. H. & TYMINSKI, L. J., 1981. Computed tomography as suspected caval thrombosis secondary to proximal extension of phlebitis from the leg. *Radiology*, *140*, 437–441.

WEYMAN, P. J., MCCLENNAN, B. L., STANLEY, R. J., LEVITT, R. G. & SAGEL, S. S., 1980. Comparison of computed tomography and angiography in the evaluation of renal cell carcinoma. *Radiology*, *137*, 417–424.

ZERHOUNI, E. A., BARTH, K. H. & SIEGELMAN, S. S., 1980. Demonstration of venous thrombosis by computed tomography. *American Journal of Roentgenology*, *134*, 753–758.

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Percutaneous transluminal angioplasty of totally occluded iliac arteries in high-risk patients

By Yukunori Korogi, M.D. and Mutsumasa Takahashi, M.D.

Department of Radiology, Kumamoto University, School of Medicine, 1-1-1 Honjo, Kumamoto 860, Japan

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ABSTRACT

Percutaneous transluminal angioplasty was performed successfully in five of six patients with complete iliac artery occlusion. All of the patients were at high risk because of various co-existing diseases. The length of occlusion ranged from 3.0 cm to 12.0 cm. No significant complications requiring surgery occurred during or after the procedures. Follow-up of patients revealed that the vessels were still patent after 3–22 months. Percutaneous transluminal angioplasty of totally occluded iliac arteries may represent the therapy of first choice even in the high-risk group

Percutaneous transluminal angioplasty (PTA) has been widely applied to short, segmental stenosis of the iliac arteries, but there have been few reported cases of PTA in totally occluded iliac arteries (Colapinto et al, 1981; Ring et al, 1982; Colapinto, 1983; Pilla et al, 1984). The application of PTA to total iliac occlusions in poor-risk patients has been considered to be less desirable because of the technical difficulty of the procedure and the possibility of distal embolisation. We have performed recanalisation and dilatation in six high-risk patients with totally occluded iliac arteries with excellent results

MATERIALS AND METHODS

Five men and one woman, aged 61–84 (average 70.8) years, underwent PTA (Table I). The symptoms had been present for more than 5 months All of the patients were at high risk because of age, hypertension, generalised arteriosclerosis, or a history of cerebrovascular disease or myocardial infarction. None could be considered for vascular surgery.

Intravenous digital subtraction angiography (DSA) was performed initially in all patients to assess the site and extent of the obstruction. Conventional arteriography was attempted at the same time as angioplasty.

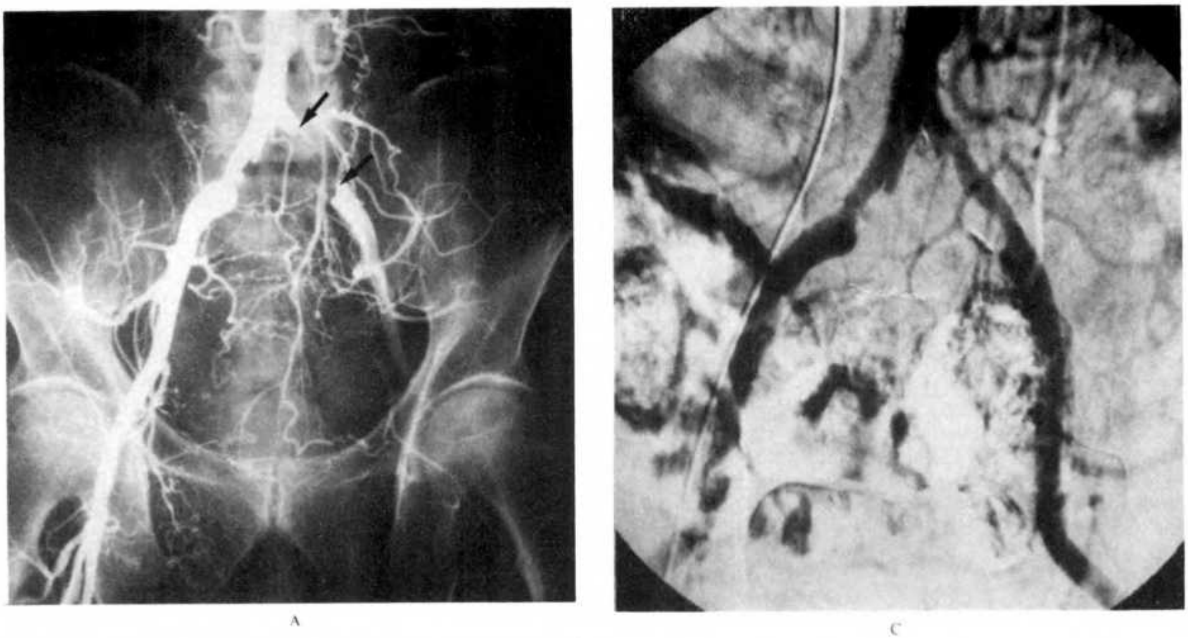
In most cases the femoral artery could be punctured without difficulty, even when pulsation was absent, and this was done via the ipsilateral femoral artery in all cases.

TABLE I

SUMMARY OF SIX PATIENTS WITH PTA OF COMPLETE ILIAC ARTERY OCCLUSION

Case	Age (years)/ Sex	Symptoms	Duration* (months)	Co-existing diseases	Site/length of occlusion	Other vascular disease/therapy	Technical result	Late results
1	77/F	Rest pain	6	Mitral stenosis, cerebral infarct	R common/ 4.0 cm	R popliteal occlusion	Success	22 months patent/no rest pain
2	84/M	Claudication	7	Cerebral infarct, myocardial infarct, diabetes	L common/ 3 5 cm	R common iliac stenosis/PTA	Success	18 months patent/ asymptomatic
3	61/M	Claudication	5	Cerebral haemorrhage	L external/ 10 5 cm	R external iliac stenosis/PTA	Success	8 months patent/ claudication improved
4	62/M	Claudication	Uncertain	Bilateral internal carotid stenosis	L common and external/ 12.0 cm	R external iliac stenosis/surgery	Failure	Surgery performed
5	66/M	Claudication	Uncertain	Hypertension	R external/ 3.0 cm	L external iliac, SFA stenosis/ PTA	Success	3 months patent/ claudication improved
6	75/M	Gangrene	13	Hypertension, amputation of R leg	L external/ 12.0 cm	L SFA occlusion/PTA	Success	3 months patent/gangrene healed

SFA = superficial femoral artery.
*Duration from the episode of exacerbation.



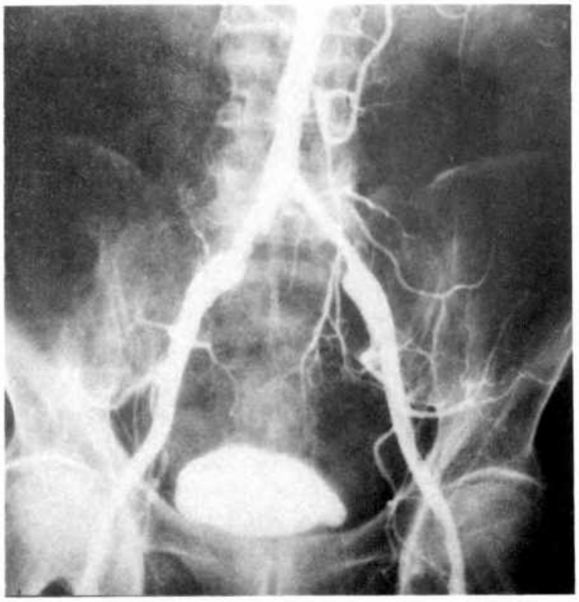


FIG. 1. *Case 2.*

(A) Before PTA: there is complete occlusion of left common iliac artery (arrows). There is also stenosis of the right common iliac artery. The late phase of the angiogram showed good run-off of left external iliac and common femoral arteries (not presented). (B) Immediately after PTA: there is good recanalisation and dilatation of the left common iliac artery. (C) Ten months after PTA: intravenous DSA confirms the patency of the left iliac artery.

Recanalisation of the obstructed segment of the iliac artery was performed by introducing a 5-French van Andel catheter with a straight, 0.035-inch guide-wire. Slow, gentle advancement of the catheter and guide-wire assembly enabled passage through the occlusion which often consisted of soft, poorly organised thrombus. Minimal force was needed to advance the guide-wire in most cases. The catheter was then exchanged for an appropriate dilating balloon catheter (usually an 8–10 mm balloon, 3–4 cm long).

After PTA, intravenous urokinase was administered at a dose of 96 000 IU/day for 7 days and ticlopidine 300 mg/day was given for 3 months. Late results were assessed by clinical examination and intravenous DSA.

RESULTS

In five cases, PTA was successfully performed, as shown by the post-PTA angiograms (Figs 1, 2). It was unsuccessful in a patient with combined occlusions of common and external iliac arteries but who subsequently underwent vascular surgery.

All patients had associated occlusive lesions of the lower extremities, which in four cases were also treated by PTA.

In Case 4, arterial perforation by the guide-wire occurred without clinical consequence. In Case 3, 10 days after PTA, follow-up examination by intravenous DSA revealed left popliteal occlusion which recanalised spontaneously, probably as a result of urokinase administration. The patient had no ischaemic symptoms during the procedure or subsequent examinations.

We encountered no significant complications requiring surgery, and follow-up for periods of 3–22 (average 10.8) months showed continued patency in the five successful cases.

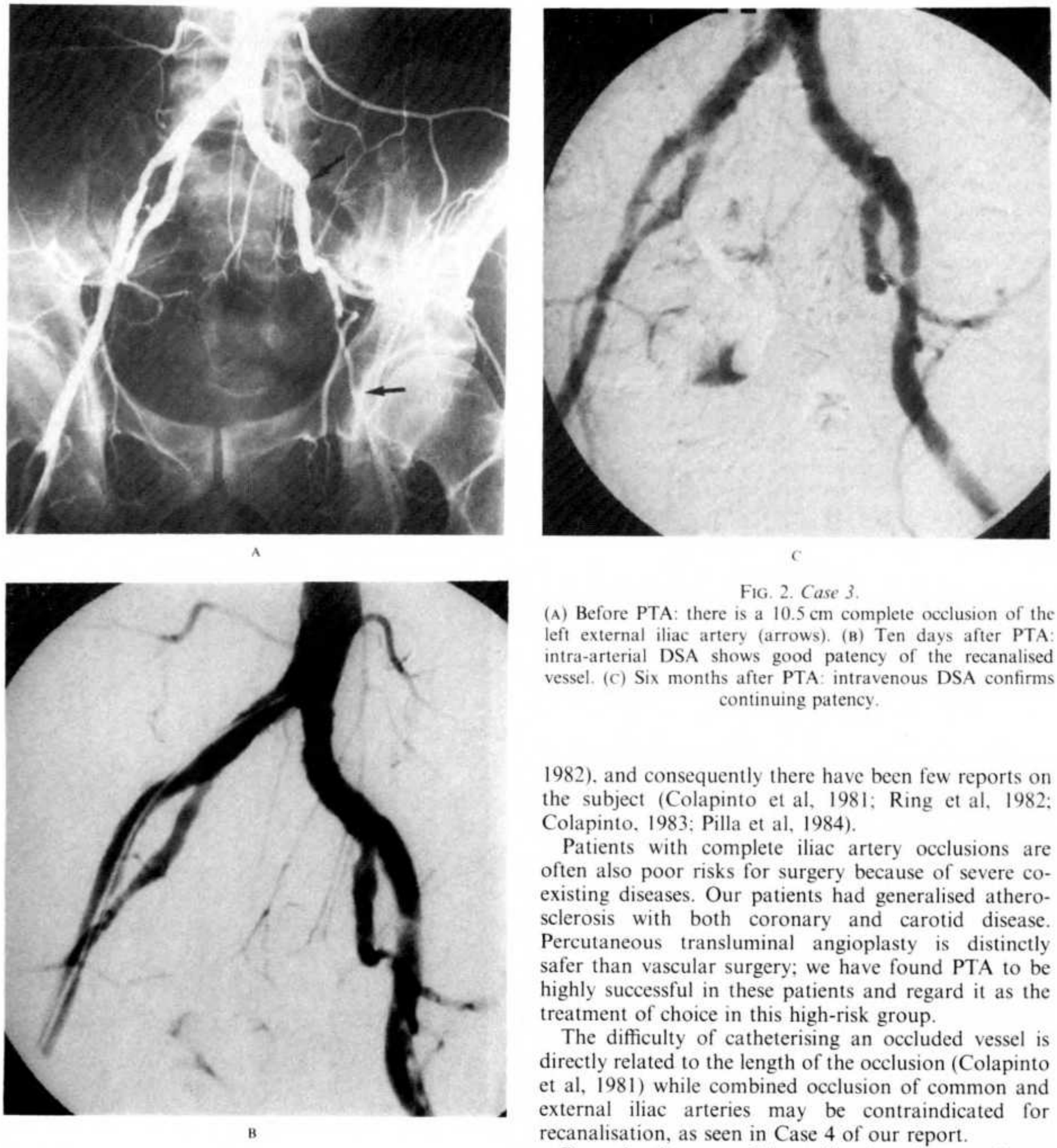


FIG. 2. *Case 3.*
(A) Before PTA: there is a 10.5 cm complete occlusion of the left external iliac artery (arrows). (B) Ten days after PTA: intra-arterial DSA shows good patency of the recanalised vessel. (C) Six months after PTA: intravenous DSA confirms continuing patency.

DISCUSSION

Localised stenoses of the iliac arteries have been treated successfully by PTA (Mortajeme et al, 1980) with a high degree of technical success and a patency rate approaching that of surgery (Spence et al, 1981; Zeitler et al, 1983). However, complete obstruction of the iliac artery has been considered to be a contraindication to PTA, since the procedure is technically difficult and may induce distal embolisation (Ring et al, 1982), and consequently there have been few reports on the subject (Colapinto et al, 1981; Ring et al, 1982; Colapinto, 1983; Pilla et al, 1984).

Patients with complete iliac artery occlusions are often also poor risks for surgery because of severe coexisting diseases. Our patients had generalised atherosclerosis with both coronary and carotid disease. Percutaneous transluminal angioplasty is distinctly safer than vascular surgery; we have found PTA to be highly successful in these patients and regard it as the treatment of choice in this high-risk group.

The difficulty of catheterising an occluded vessel is directly related to the length of the occlusion (Colapinto et al, 1981) while combined occlusion of common and external iliac arteries may be contraindicated for recanalisation, as seen in Case 4 of our report.

Recently, the successful combination of streptokinase infusion and PTA were reported in the treatment of iliac artery occlusion (Auster et al, 1984; Lammer et al, 1985). These reports stressed that this combination was a safer and more effective technique in unilateral iliac occlusion. Our patients had not undergone intra-arterial thrombolytic therapy, but received intravenous infusion of urokinase. The advantages of our method are felt to be the speed and simplicity of the technique and avoidance of bleeding complications. High risk of peripheral embolisation has been reported after treating iliac occlusion by PTA (Ring et al, 1982), but peripheral embolisation may occur with thrombolytic therapy alone. Recent experience has confirmed that thrombosis usually occurs superimposed on a chronic underlying stenosis and it may be a disadvantage that an underlying stenosis cannot be demonstrated by our method. Since our experience has so far been limited, more data will be required before the proper indications for management of these patients can be finally determined.

REFERENCES

AUSTER, M , KADIR, S., MITCHELL, S. E., WILLIAMS, G. M , PERLER, B. A., CHANG, R. & WHITE, R. I., JR, 1984. Iliac artery occlusion: management with intrathrombus streptokinase infusion and angioplasty. *Radiology, 153*, 385–388

COLAPINTO, R. F., 1983. Long-term results of iliac and femoropopliteal angioplasty. In *Percutaneous Transluminal Angioplasty*. Ed by C T Dotter, A R Gruntzig, W. Schoop & E. Zeitler, (Springer-Verlag, Berlin) pp. 202–206.

COLAPINTO, R. F., HARRIES-JONES, E. P. & JOHNSTON, K. W., 1981. Percutaneous transluminal recanalization of complete iliac artery occlusions. *Archives of Surgery, 116*, 277–281.

LAMMER, J., PILGER, E , JUSTICH, E., NEUMAYER, K. & SCHREYER, H., 1985. Fibrinolysis in chronic arteriosclerotic occlusions: intrathrombotic injections of streptokinase. *Radiology, 157*, 45–50.

MORTAJEME, A., KEIFER, J W., & ZUSKA, A. J., 1980. Percutaneous transluminal angioplasty and case selection. *Radiology, 135*, 573–581.

PILLA, T. J., PETERSON, G J., TAHTANA, S., LANG, E R. & WOLVERSON, M. K., 1984. Percutaneous recanalization of iliac artery occlusions: an alternative to surgery in the high-risk patient. *American Journal of Roentgenology, 143,* 313–316

RING, E. J., FREIMAN, D. B., MCLEAN, G. K & SCHWARZ, W., 1982. Percutaneous recanalization of common iliac artery occlusions. an unacceptable complication rate? *American Journal of Roentgenology, 139*, 587–589.

SPENCE, R. K , FREIMAN, D. B., GATENBY, R., HOBBS, C. L , BARKER, C. F , BERKOWITZ, H. D., ROBERTS, B., MCCLEAN, G , OLEAGA, J. & RING, E. J., 1981. Long-term results of transluminal angioplasty of the iliac and femoral arteries *Archives of Surgery, 116*, 1377–1386.

ZEITLER, E., RICHTER, E. I., ROTH, F. J. & SCHOOP, W., 1983. Results of percutaneous transluminal angioplasty. *Radiology, 166*, 57–60.

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The radiation dose to the lens in radiology of the orbit

By A. Montanara, M.D., *R. Pani, Ph.D., †R. Pellegrini, Ph.D., N. S. A. Polli, M.D. and †S. Soluri, Ph.D.

Department of Ophthalmology, Radiology Section, and *Health Physics Department, University "La Sapienza", Rome, Italy, and †SSLPS CNR, Rome, Italy

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ABSTRACT

This paper describes research into measurement and reduction of the radiation dose to the lens during various examinations, namely skull and orbit, optic canal and optic strut, superior and inferior orbital fissure, localisation of foreign bodies in the eye, calcifications, orbital fractures, macrodacryography and orbital venography. Using rare-earth screens and high-sensitivity films, without an antiscattering grid, and with an added filtration of 0.5 mm Cu, it is possible to reduce the radiological risk during all investigations involving skull, orbit and eyeballs, while maintaining a good image quality. Particularly in those examinations with direct magnification (macrodacryography and venography, foreign bodies in the eye, orbital fractures), the dose to the lens is very low: less than 0.2 mGy/radiograph.

Dose reduction to patients during various radiological examinations is important and physicists and radiologists have devoted particular attention to it, both nationally and internationally. In particular, it is well known that the different structures of the eye can be injured by ionising radiation, producing changes in the metabolism and morphology of the various components of the eyeball. The lens of the eye is considered to be the most critical organ.

The intensity of the effects varies in relation to the dose received by the eye and can be assumed to follow the pattern of inflammation and degeneration of the conjunctival epithelium, striated keratitis, necrosis and desquamation of the corneal epithelium with neovascularisation, iris hyperaemia, opacities located in the anterior pre-equatorial region of the lens (germinal area) due to coagulated proteins, and neuroretinal changes subsequent to vascular damage (disorganisation of cones and rods, ganglionic chromatolysis, and optic nerve demyelinisation).

We have described elsewhere (Ballesio et al, 1985) an investigation into reduction of the dose to the lens in ophthalmological radiology, based on analysis of the transmitted spectrum with a new detection system using a CdTe detector (Di Castro et al, 1984). Preliminary data from work on a phantom showing the dose reduction to the lens have already been published (Ballesio et al, 1985). In that paper it is shown that, with the addition of a 0.5 mm Cu filter, it is possible to obtain a three-fold dose reduction in comparison with one using a filtration of 2.5 mm Al, without impairing the image quality. The present paper describes further measurements of the dose absorbed from the lens in man during the radiological investigation of the skull and orbit in order to evaluate the practical applications of the research to ophthalmological radiology.

MATERIAL AND METHODS

A 125 kV max Duratron rotating-anode X-ray tube with microfocus (0.3 mm and 1.0 mm) was used. The primary beam was filtered with 0.5 mm Cu. Rare-earth screens and suitable screen–film combinations were used. In particular, gadolinium oxisulphide screens (3M Trimax T16) were used with high-sensitivity films (3M XM and XD).

In the dose measurements a MDH dosemeter was used with a 6 cm^3 chamber with an accuracy to X rays within 5%. It was used to calibrate lithium fluoride thermoluminescent dosemeters (TLDs). The chamber and dosemeters were irradiated with a 100 kV X-ray beam filtered with 0.5 mm Cu to different exposure values. The dosemeters were placed on a plexiglass phantom 1 m from the X-ray source.

To measure the doses on patients, the lithium fluoride TLDs were put on the eyelids of patients subjected to radiographic examination of the skull, with or without direct magnification. Macroradiography reduces the radiation to the unprotected eyes because the stationary grid is not needed. With this method the increase in dose due to the greater focus–detector distance is largely compensated for by the dose reduction obtained by removing the grid, which generally has a grid factor from 2 to 5 (Drexler et al, 1984). Moreover, misalignment and/or incorrect focus-to-grid distance can result in drastically higher grid factors and, consequently, a higher entrance dose to the patient.

In ophthalmological radiology, magnification is often used in both orbital traumatology and looking for foreign bodies, in dacryography and angiography (Lloyd & Ardagh, 1972). In our examinations the focus–skin distance was 1 m and the distance between subject and film was 45 cm with a 1.5 magnification factor. The dosemeters were put on the eyelids, providing a skin dose instead of the depth dose. A correction for the depth of the eye lens was then

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Requests for reprints: A. Montanara, M.D., Clinica Oculistica, Reparto di Radiologia, Policlinico Umberto I, 00161 Roma, Italia.

applied. To this end, the attenuation of the incident detected spectrum (Ballesio et al, 1985) as it traverses 3 mm of tissue was calculated. Narrow-beam conditions (*i.e.* no scatter component) were assumed and the mass attenuation coefficients for soft tissue listed by the Hospital Physicists' Association (Birch et al, 1979) were used. Correction from 8% to 12% has been calculated, respectively, for spectra of 100 kV down to 65 kV.

Examinations *in vivo* were carried out with different collimation cones and a 0.5 mm Cu filter. 3M Trimax T8 screens and XD films were used for plain radiography of the skull and orbit, and 3M Trimax T16 screens with XD or XM films for macrodacryography and venography.

RESULTS

Table I shows the results of the dose measurements on the human eyeball, and Fig. 1 shows that a good image quality was maintained. Plain radiographic examination of the skull (four projections) implies a dose of 1.58 mGy to the lens, the examination of the orbit and eyeball (two projections) implies a dose of 0.77 mGy and antero-posterior (AP) conventional tomography (seven layers), a dose of 7.35 mGy. In macrodacryography performed without a stationary grid and using the magnification technique, the dose to the lens is 0.60–0.83 mGy for four radiographs, depending on the type of film used (Table I). In this case, to minimise the error due to the minimum dose detectable by the LiF dosemeters, they were exposed four times on a series of different patients.

DISCUSSION AND CONCLUSION

It is possible to reduce the dose to the lens by changing the technical parameters, using appropriate screen–film combinations, filtering the X-ray beam and leaving out the grid. In macrodacryography and venography the dose is further reduced because the scattered radiation decreases with the greater subject–film distance. In examinations with magnification, dosimetry on phantoms shows (Table II) how it is possible to achieve a lens dose of 0.48 mGy/film using suitable screen–film combinations without added filtration. The dose is further reduced to 0.28 mGy/film by adding a 4.25 mm Al + 0.1 mm Cu filter and to 0.23 mGy with a 0.2 mm Cu filter. Lastly, the dose is reduced to 0.17 mGy with a 0.5 mm Cu filter.

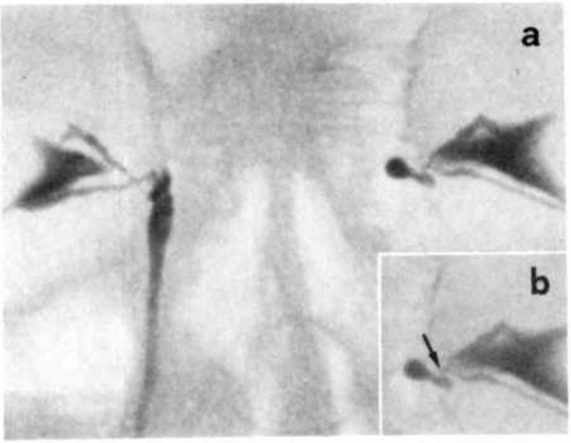

FIG. 1.

(a) Macrodacryography performed only with inherent filtration (1.5 mm Al). (b) The same case examined with added filtration of 0.5 mm Cu.

The added filtration, which requires a proportional increase in mAs, has little effect on the image quality, just lowering the contrast tonality on the film without reducing the definition (see Fig. 1). The disadvantage of the modest contrast reduction is widely compensated for by the dose reduction and it has no influence on the informative value of the radiograph, that is to say its practical utility in diagnosis. If the information content is adequate, it is better, in our opinion, to have a "less fine" examination with a lower radiation dose rather than a "finer" one with a much higher dose to the patient.

It is known that good radiographic quality depends on minimal fluctuation in X-ray beam intensity, a low

TABLE I

RADIATION DOSE TO THE LENS IN ORBITAL INVESTIGATIONS IN MAN (FILTRATION 0.5 MM CU)

Examination	Trimax screen	3M film	Grid	kVp	mAs	Absorbed dose	
						mGy/examination	mGy/radiograph
Standard skull projection, four films	T8	XD	G	65–75	80	1.58 ± 4%	0.39 ± 4%
AP tomography of the orbit, seven films	T8	XD	G	75	100	7.35 ± 1%	1.05 ± 1%
Localisation of foreign bodies in the eye, two films	T8	XD	G	75–80	80	0.77 ± 5%	0.38 ± 5%
				65	65		
Macrodacryography, four films	T16	XM	—	100	4	0.60 ± 7%	0.15 ± 5%
		XD	—		6	0.83 ± 5%	0.20 ± 5%
Venography, four films	T16	XM	—	100	4	0.60 ± 7%	0.15 ± 7%
		XD	—		6	0.83 ± 5%	0.20 ± 5%

TABLE II

RADIATION DOSE TO THE LENS IN ORBITAL MAGNIFICATION (HUMANOID PHANTOM)*

kVp	mAs	Added filtration	Absorbed dose (mGy/radiograph)
95	3	1.5 mm Al (inherent)	0.48±8%
95	6	4.25 mm Al+0.1 mm Cu	0.28±10%
100	4	0.2 mm Cu	0.23±10%
100	6	0.5 mm Cu	0.17±12%

*No grid. Screen–film system = rare-earth intensifying screen (T16) used with high-speed sensitive film (Trimax XM)

kinetic penumbra (produced by a lower exposure time) and a low geometric penumbra (produced by an increased focus–skin distance and by a very small focal spot). Macrodacryography and orbital angiography are examinations requiring a small focal spot, very short exposure time, serial radiographs, direct magnification and subtraction. In these examinations there is the particular need to reproduce very fine structures which are filled by the contrast medium and which are in motion. The lowest dose to the lens was 0.15 mGy/radiograph. This value is equal to or less than those measured in dacryoscintigraphy by other workers (Robertson et al, 1979; Doucet et al, 1982; Polli et al, 1985). It is 20 times less than the skin dose in skull examinations (Rogers, 1969; Bergström et al, 1977) using traditional screens and films with a grid, and it is half that in a plain radiographic examination of the orbit performed with rare-earth screens and high-sensitivity films (Table I).

The low irradiation to the lens in both macrodacryography and dacryoscintigraphy entitles us to say that the choice between the two investigations need not be conditioned by the radiation risk (about the same and extremely low for both), but by the different indications that they present. For investigating the physiology of tear drainage and in the study of lacrimal functional disorders, dacryoscintigraphy is extremely valuable; in lacrimal malformations, obstructive epiphora and post-operative follow-up, macrodacryography has the greatest diagnostic certainty

It is possible, therefore, to conclude that the irradiation of the orbit during different examinations (skull and orbit, optic canals and orbital fissures, foreign body localisation, orbital fractures, microcalcifications, angiography and particularly macrodacryography) does not represent a radiological hazard, providing that the examinations are carried out using the correct technique.

REFERENCES

BALLESIO, P. L., PANI, R., PELLEGRINI, R. & FURETTA, G., 1985. Dose reduction and image optimisation in ophthalmological radiology. *British Journal of Radiology, Suppl. 18*, 124–126

BERGSTRÖM, K., JORULF, H & LÖFROTH, P. O., 1977. The eye lens. Some aspects of the radiation dose and protection of the patients and the personnel in pediatric radiology. *Annales de Radiologie, 20*, 55–61.

BIRCH, R., MARSHALL, M. & ARDRAN, G. M., 1979. *Catalogue of Spectral Data for Diagnostic X-rays*. SRS30 (Hospital Physicists' Association, London).

DI CASTRO, E., PANI, R., PELLEGRINI, R. & BACCI, G., 1984. The use of CdTe detectors for the qualitative analysis of diagnostic x-ray spectra *Physics in Medicine and Biology, 29*, 1117–1131

DOUCET, T W., HURWITZ, J J. & CHIN-SANG, H., 1982 Lacrimal scintillography: advances and functional applications. *Survey of Ophthalmology, 27*, 105–113

DREXLER, G., PANZER, W., WIDENMAN, L., WILLIAMS, G. & ZANKL, M., 1984. The calculation of dose from external photon exposures using reference human phantoms and Monte Carlo methods. Part III. *GSF Bericht, 1026*, 6.

LLOYD, G. A. S. & ARDAGH, J, 1972. Adaptation of a standard skull table for enlargement angiography and dacryocystography. *X-ray Focus, 12*, 16–18

POLLI, N. S. A., GIBOLDI, G., MARULLO, M., NOVACCO, V., YAHYA, M., PANI, R. & PELLEGRINI, R., 1985. La riduzione della dose in radiologia oftalmologica. *Clinica Oculistica e Patologia Oculare, 3*, 207–211.

ROBERTSON, J. S., BROWN, M. L & COLVARD, D M, 1979 Radiation absorbed dose to the lens in dacryoscintigraphy with ^{99}TcO$_4{}^{-1}$. *Radiology, 133*, 747–750

ROGERS, R. T, 1969. Radiation dose to the skin in diagnostic radiography. *British Journal of Radiology, 42*, 511–520.

Book review

Atoms, Radiation, and Radiation Protection By James E Turner, pp xii+324, 1986 (Pergamon Press, New York), $60.00 hard cover, $32.50 soft cover.

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0–08–031949 (soft cover)

As its title suggests, this book is principally about atomic and nuclear structure, ionising radiations and radiation protection. The text has been written from material used by the author over many years in teaching courses dealing with health physics, microdosimetry and the application of Monte Carlo techniques to radiation protection. The interaction of charged particles and photons with matter, as well as methods of detecting these radiations, are described thoroughly. The chemical and biological effects of radiation are summarised clearly, as are the fundamentals of radiation protection and internal dosimetry. The book will be of interest to students and professionals in radiation physics, nuclear engineering and environmental health services. Although the author does not deal specifically with radiotherapy and nuclear medicine, the subject matter covered provides useful basic information for anyone interested in these subjects.

The book is well written. It has a clear format and is illustrated with appropriate, simple line drawings and photographs. Although SI units are employed in much of the book, traditional units of radiation dosimetry are also used. Within the text there is a comprehensive selection of questions with detailed solutions to illustrate the principles of the main subjects. At the end of each chapter there are 30 to 50 additional questions which students will find helpful to work through. However, it would have been apposite to have included answers to those questions which have a numerical solution.

I found the best chapters to be those dealing with the chemical and biological effects of radiation, radiation protection criteria and standards, and the section dealing with internal dosimetry and radiation protection. The former chapter includes helpful examples of Monte-Carlo calculated charged-particle track segments in water, which are presented pictorially: these are used with effect to illustrate the sequential development and diffusion of reactive species in relation to the action of radiation on DNA.

For departments involved in teaching radiation physics to undergraduates, this is a good book to purchase for the departmental library. I suspect that the cheaper soft-cover binding (provided by the publishers for review!) will be found to be the better buy for most purchasers.

COLIN H. JONES

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Clinical evaluation of anti-alpha-fetoprotein radioimmunodetection

By C. E. Chapman, B.Sc., M.R.C.P., *D. S. Fairweather, Ph.D., M.R.C.P., A. A. Keeling, Ph.D., †S. T. Chandler, B.Sc., M.Sc., ‡P. W. Dykes, M.D., F.R.C.P. and A. R. Bradwell, F.R.C.P., M.R.C.Path.

Immunodiagnostic Research Laboratory, Department of Immunology, The Medical School, Vincent Drive, Birmingham B15 2TJ; *Department of Geriatric Medicine, University of Manchester, Manchester M20 8LR; †Department of Nuclear Medicine, Queen Elizabeth Hospital, Birmingham B15 2TH; ‡The General Hospital, Steelhouse Lane, Birmingham B4 6NH

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ABSTRACT

Anti-alpha-fetoprotein (AFP) radioimmunodetection was performed in response to clinical requests in 16 patients In two patients, assessment of a known tumour was required, the anti-AFP scans were accurate and provided useful clinical information in both cases In the remaining 14 patients the request was for localisation of suspected recurrent tumour. Accurate information was provided in four of these patients. In this latter group, various conventional methods of investigation had failed to disclose the site of recurrence. However, of a total of 21 sites reported as positive in these 14 patients, eight proved to be false positives Two false negative results also occurred in this group and nine could not be evaluated. Although occasionally patients were usefully scanned, improvements are necessary before consistently reliable information can be obtained using this technique

The technique of radioimmunodetection has been applied, with some success, to the localisation of tumours producing alpha-fetoprotein (AFP) (Kim et al, 1980; Halsall et al, 1981; Javadpour et al, 1981). There are occasional reports of tumour detection by radioimmunodetection preceding confirmation by other methods (Kim et al, 1980; Halsall et al, 1981) but the majority of positive scans merely permit the visualisation of known tumour areas. The potential clinical application of this technique was suggested by these preliminary studies and in the past 5 years we have received 16 requests for anti-AFP scans. Each request was prompted by the requirement for further information for the purpose of resolving a clinical problem. This paper details our results in these patients.

METHODS

Patients

Sixteen patients were scanned: all had had previous tumours with an established histological diagnosis. The diagnoses were malignant teratoma of testis in 11, yolk sac tumours in two, sacrococcygeal teratoma in one, hepatoblastoma in one and pancreaticoblastoma in one. The requests for anti-AFP scans fell into two groups:

(A) assessment of a known mass (two patients);
(B) localisation of a presumed recurrence (14 patients).

In the latter group the primary tumours had been surgically removed. A subsequent search for recurrent tumour had been prompted by a rising serum AFP in the majority of patients. Investigation of these patients by various conventional techniques, which had been available to the referring physician, had failed to identify a site of recurrence. These included computed tomography (CT), ultrasound and conventional radiography.

Antibody preparation

Hyperimmune sheep antiserum was raised against human AFP purified from amniotic fluid. The antiserum was solid-phase adsorbed to remove antibodies reacting with normal human serum and tissue components. Specificity for AFP was confirmed by immunoelectrophoresis and immunohistochemistry. An immunoglobulin-G fraction was prepared by ammonium sulphate precipitation and subsequent ion exchange chromatography (DEAE cellulose). Batches of antibody were passed through a 0.2 μm filter and were tested for pyrogenicity by an independent laboratory. The antibody was radiolabelled with iodine 131 (Amersham International, code IBS 30) as described previously (Fairweather et al, 1983a) using a modification of the chloramine-T method of Hunter and Greenwood (1962) to a specific activity of 0.18–0.37 MBq (5–10 μCi) per μg. Radiolabelled antibody was separated from free iodine by gel filtration (Sephadex G25). The antibody was then centrifuged overnight at 20 000 *g* and repeat 0.2 μm filtration was performed. Each patient was given approximately 3 μg/kg (usual adult dose 37–74 MBq, 1–2 mCi)

Antibody administration

Informed consent was obtained either from the patient or, in the case of children, from both parents. Thyroid and gastric uptake of ^{131}I was blocked by treatment with oral potassium iodide, 60 mg tds for 1 week, and oral potassium perchlorate 600–800 mg 1 h before antibody injection and 1 h before each scan. A 20 μg test dose of antibody was administered intravenously 15 min before proceeding to injection of the complete dose. No adverse reactions were encountered.

Scanning procedure

Scans were recorded 24 h and 48 h after ^{131}I anti-AFP injection; 37 MBq (1 mCi) technetium-99m-labelled human serum albumin and 37 MBq sodium pertechnetate-^{99}Tc^{m} were injected intravenously 5 min and 30 min, respectively, before each scan for the purpose of image subtraction (Deland et al, 1980). Simultaneous ^{131}I and ^{99}Tc^{m} images of the chest and anterior, posterior and lateral abdomen were obtained either with a Searle LFOV gamma camera or with a CGR Gammatome with a medium-energy, parallel-hole collimator and linked to a DEC PDP 11 computer. Counts were acquired for five minutes from each view. Technetium subtraction images were generated after applying a nine-point smooth once to each image and then normalising over the heart. A second subtracted image was then produced which was thresholded to display only significant counts. Significant counts were defined as more than two standard deviations above the background noise level as calculated for a reference area over the lung (Fairweather et al, 1983b). Each scan was reported by two of us (D S.F and A.R.B. or C.E.C. and A.R.B.); opinions were in close agreement.

Results

A summary of results is presented in Table I. The anti-AFP scans were accurate and provided useful clinical information in both patients in whom assessment of a known mass was required (Group A). The site of tumour recurrence was accurately localised in four of the 14 patients who had been referred with presumed recurrence (Group B). Computed tomography had failed to identify tumour in three of these four patients and had not been performed in the fourth. Twenty-one areas were reported as positive or possible positive in Group B, eight proved subsequently to be false positives and nine could not be evaluated due to lack of follow-up information.

An example of an anti-AFP scan is shown in Fig. 1. The patient scanned was a child (Case 11) with presumed recurrent hepatoblastoma. Abdominal CT had failed to identify the site of recurrent tumour on two occasions. Marked hepatic uptake of ^{131}I anti-AFP is apparent in both subtraction images (1c and 1d) Small areas of increased uptake are also seen in the left hypochondrium and adjacent to the bladder. The latter two areas were reported as possible positive (+/−).

TABLE I

Summary of results of anti-alpha-fetoprotein scans in 16 patients

Case	Age (years)	Diagnosis*	Group	Serum AFP (IU/ml)	AFP scan†	Confirmation	Scan accuracy
1	24	MTT	A	10	− (chest)	− (histology)	True −ve
2	39	MTT	A	120	+ (chest)	+ (follow-up)	True +ve
					+ (abdomen)	+ (follow-up)	True +ve
3	45	MTT	B	42	+/− (chest)	None	Unknown
4	27	MTT	B	50	+ (abdomen)	? (responded to chemotherapy)	Unknown
5		MTT	B	57	+ (bone)	+ (radiography)	True +ve
6	6	Ovarian yolk sac tumour	B	60	+ (abdomen)	− (laparotomy, also undetected tumour noted)	False +ve False −ve
7	24	MTT	B	62	+ (chest)	− (thoracotomy, also undetected tumour noted)	False +ve False −ve
8	34	MTT	B	100	+/− (abdomen)	− (laparotomy)	False +ve
9	44	MTT	B	120	+ (bone)	+ (bone scan)	True +ve
10	2	Yolk sac tumour	B	190	+/− (chest)	None	Unknown
11	4	Sacrococcygeal teratoma	B	96	+ (iliac nodes)	− (follow-up)	False +ve
					+ (para aortic)	− (follow-up)	False +ve
12	20	MTT	B	<10	+ (epigastrium)	None (pt died 4 months after scan no post-mortem)	Unknown
					+/− (iliac nodes)		Unknown
					+/− (mediastinum)		Unknown
13	30	MTT	B	400	+ (left testis)	− (histology)	False +ve
					+ (para aortic)	+ (CT)	Unknown
					+/− (mediastinum)	None	Unknown
14	23	MTT	B	241	+ (para aortic)	+ (laparotomy)	True +ve
15	2	Pancreaticoblastoma	B	365	+ (mediastinum)	None	Unknown
16	2	Hepatoblastoma	B	>1000	+ (liver)	+ (laparotomy)	True +ve
					+/− (L hypochondrium)	−	False +ve
					+/− (pelvis)	−	False +ve

*MTT = malignant teratoma of testis

†+/− = possible positive.

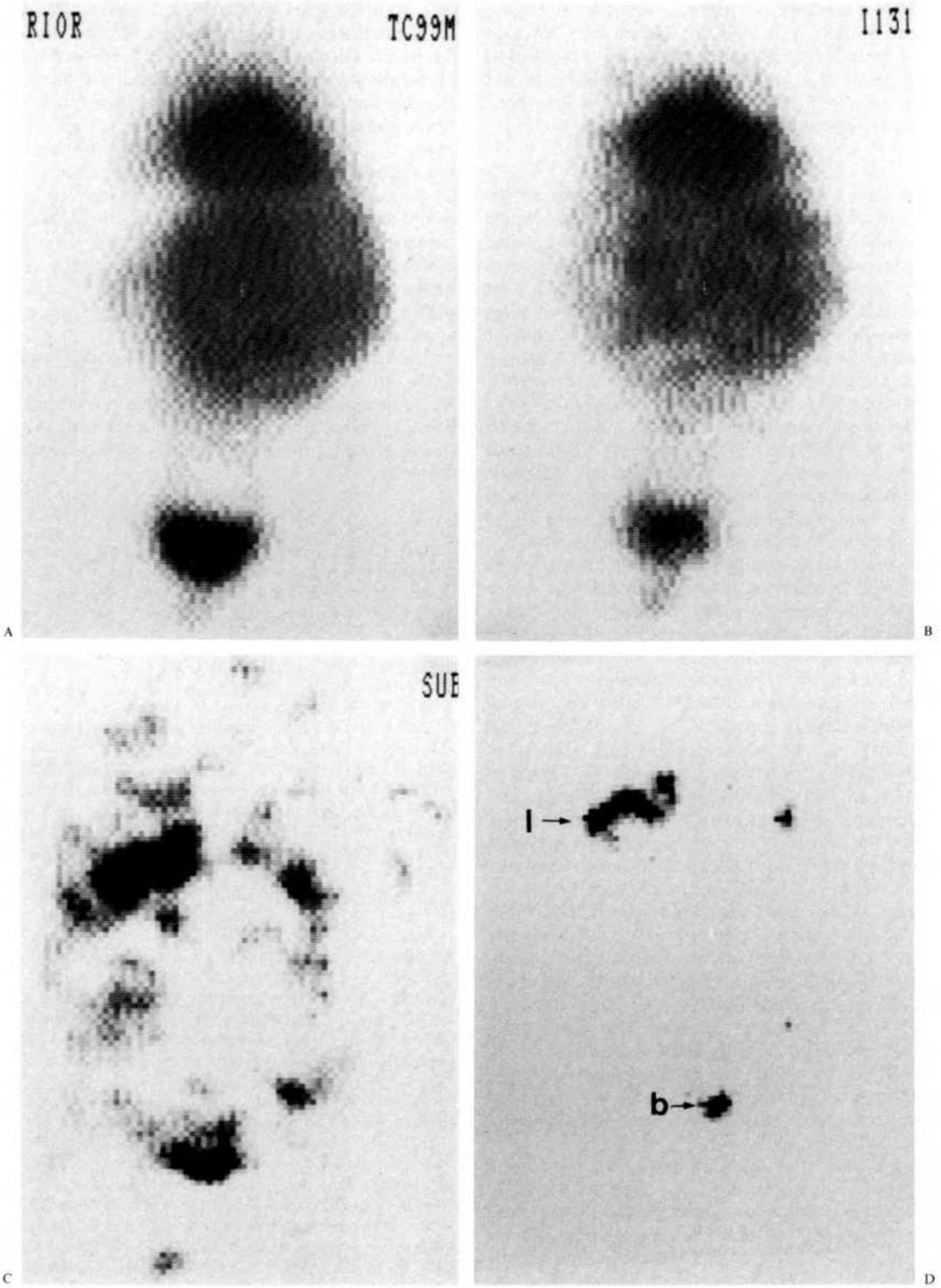

FIG. 1. *Case 11.*

AP views of the abdomen. (A) ^{99}Tc^{m} scan, (B) ^{131}I anti-AFP scan, (C) subtraction image (after normalisation over the heart), (D) subtraction image thresholded to display significant counts only: l = liver, b = bladder.

This scan was repeated after 2 months and gave consistent results. A subsequent laparotomy revealed recurrent hepatoblastoma in the liver, confirming this as a true positive scan area. Recurrent tumour was not found at either of the two smaller sites which were, therefore, false positive artefacts.

DISCUSSION

The diagnostic value of the scans was poor in the majority of patients, although there were some which were considered useful. For instance, in the two patients who were scanned with known masses the scans provided useful results. In the other patients only four scans provided accurate tumour localisation and there were many false positives and negatives. It should be emphasised, however, that in this group previous attempts at tumour localisation using more conventional investigations had all been unsuccessful.

Clearly, in any diagnostic test, false positive results cause the most difficulty. They occurred in our scans for several reasons and the subtraction technique appears to be of particular relevance. This technique is used to provide image enhancement and is necessary in radioimmunodetection because only a small percentage of the injected dose of labelled antibody binds to the tumour The subtraction isotope mimics the distribution of the tumour-seeking antibody but has a different photon emission energy. Although this technique improves contrast it leads to difficulties. The localising nuclide (^{131}I) has more energetic γ rays than the subtracting nuclide (^{99}Tc^{m}) and the greater penetration results in artefacts. The *in-vivo* biological characteristics of the two isotopes are dissimilar, causing differential organ accumulation. This leads to false hot and cold areas. For example, the bladder always contains an excess of free iodine or technetium, which leads to hot or cold areas Inequalities may also occur around the heart or stomach, although the latter can usually be blocked with a combination of potassium iodide and potassium perchlorate. The process of subtraction, while improving contrast, also introduces statistical fluctuations without increasing the signal, *i.e.* the signal-to-noise ratio is reduced. Many of these problems occurred in our scans.

Apart from subtraction-generated artefact, non-specific accumulation of radio-labelled antibody due to cross-reactivity with normal tissue components may cause false positive results. This was minimised by extensive antibody adsorption and immunohistochemical assessment

Clearly, to find more application, these scans need to be improved. The single, most important determinant of a successful radioimmunodetection scan is the ratio between the amount of radio-labelled antibody in the tumour compared with that in the surrounding normal tissue. We were unable to measure tissue ratios in this study but those achieved in radioimmunodetection are generally less than five and usually nearer two and various manipulations to date have failed to improve on this ratio (Bradwell et al, 1985). Theoretical considerations applicable to radioimmunodetection have been discussed (Bradwell et al, 1985) and predict that, excluding uptake ratio, the most important factor which can be improved is the absolute count rate of the tumour-locating isotope. Our scan count densities, using ^{131}I, are often less than 100/cm^2. The theoretically predicted improvement in scan quality to be gained from trebling the count density, for example, would be the equivalent of doubling the uptake ratio. Increases in count density may be achieved by prolonging count acquisition times, within practical limits, and by increasing the dose of ^{131}I anti-AFP within safety guidelines. This may provide a useful approach to future scan improvement.

Antibody scans have potential application in diverse fields. In contrast to other scanning methods, the technique offers functional information (antigen production) rather than merely structural detail. Attention to the existing problems may allow this potential to be achieved

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REFERENCES

BRADWELL, A. R., FAIRWEATHER, D. S., DYKES, P. W., KEELING, A., VAUGHAN, A. & TAYLOR, J., 1985. Limiting factors in the localization of tumours with radiolabelled antibodies *Immunology Today, 6,* 163–170.

DELAND, F. H., KIM, E. E., SIMMONS, G. & GOLDENBERG, D M, 1980 Imaging approach in radioimmunodetection *Cancer Research, 40,* 3046–3049.

FAIRWEATHER, D. S., BRADWELL, A. R., WATSON-JAMES, S. F, DYKES, P W, CHANDLER, S & HOFFENBERG, R., 1983a Detection of thyroid tumours using radiolabelled thyroglobulin. *Clinical Endocrinology, 18,* 563–570

FAIRWEATHER, D. S., IRWIN, M, BRADWELL, A R, DYKES, P W & FLINN, R M, 1983b. Computer analysis of antibody scans *Protides of the Biological Fluids, 31,* 285–288.

HALSALL, A. K., FAIRWEATHER, D S, BRADWELL, A. R, BLACKBURN, J C, DYKES, P. W., HOWELL, A, REEDER, A. & HINE, K. R., 1981. Localisation of malignant germ-cell tumours by external scanning after injection of radiolabelled anti-alphafoetoprotein. *British Medical Journal, 283,* 942–944.

HUNTER, W. M. & GREENWOOD, F. C., 1962 Preparation of iodine-131 labelled human growth hormone of high specific activity. *Nature (London), 194,* 495–496

JAVADPOUR, N., KIM, E., DELAND, F H., SALYER, J. R., SHAH, U & GOLDENBERG, D. M., 1981 The role of immunodetection in the management of testicular cancer. *Journal of the American Medical Association, 246,* 45–49.

KIM, E. E., DELAND, F. H., NELSON, M. O., BENNETT, S., SIMMONS, G., ALPERT, E. & GOLDENBERG, D. M., 1980. Radioimmunodetection of cancer with radiolabelled antibodies to alpha-fetoprotein *Cancer Research, 40,* 3008–3012

1986, *The British Journal of Radiology*, 59, 1179–1184

A new technique for xenon-133 ventilation imaging in the diagnosis of pulmonary embolism

By *B. L. Diffey, Ph.D., F.Inst.P., C. J. Gibson, B.A., M.Sc. and L. E. Scott

Regional Medical Physics Department, Dryburn Hospital, Durham DH1 5TW

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ABSTRACT

A new approach to ventilation imaging of the lung using ^{133}Xe in patients with suspected pulmonary embolism is described. Three inhalation images are obtained in the postero-anterior, right posterior oblique and left posterior oblique projections, respectively, and each image contains 140–180 kcounts. The technique is quick and simple and needs neither an oxygen supply nor a spirometer. It combines the multiple views characteristic of krypton imaging with the ease of availability of xenon.

The role of pulmonary scintigraphy as a sensitive and non-invasive method for the diagnosis of pulmonary embolism (PE) is well documented (McNeil, 1976; Alderson & Line, 1980; Neumann et al, 1980; Blinder & Coleman, 1985). The investigation normally consists of two parts: perfusion imaging using either human albumin microspheres or macroaggregates labelled with ^{99}Tc^{m}; and ventilation imaging using either ^{133}Xe, ^{127}Xe, ^{81}Kr^{m} or radioaerosols.

Xenon 133 is perhaps the most commonly used radionuclide for ventilation studies and, when combined with the perfusion images (V/Q imaging), significantly increases the diagnostic accuracy for detecting pulmonary embolism (Alderson et al, 1976). The "standard" technique for performing the ^{133}Xe ventilation scan is as follows (Alderson & Line, 1980). The patient sits with his back to the gamma camera. About 300–700 MBq ^{133}Xe is injected into tubing near the patient's mouthpiece or mask after the patient completes a routine tidal exhalation. An inhalation is taken to vital capacity and the patient holds his breath until a 25–75-kcount image has been obtained. The gas is then re-breathed for 3–5 min from a closed reservoir containing a CO_2 absorber. After this period, an equilibrium image is obtained. The washout phase is now initiated and images are taken every minute until the gas clears from the lungs. The apparatus needed to carry out this investigation includes a spirometer, oxygen supply, and an exhaust collection system or charcoal trap (Neumann et al, 1980).

Since the interpretation of V/Q studies in the diagnosis of pulmonary embolism relies on a mismatch between perfusion abnormalities and ventilation abnormalities, we describe here a new approach to ^{133}Xe ventilation imaging in an attempt to optimise the probability of detecting a non-matched perfusion defect.

Our technique is based upon two premises:

(a) multiple inhalation views increase the probability of detecting a non-matched perfusion defect compared with the conventional single posterior projection;
(b) obtaining images with considerably more than the typical number of 25–75 kcounts in the posterior inhalation view increases the confidence with which ventilation defects can be detected.

In addition, the technique described below needs neither an oxygen supply nor spirometer. Also, if ready access to the outside air is available, the need for either an exhaust collection system or a charcoal trap is obviated since the exhalation tubing can be connected directly to an exit port in an outside wall. This minimises dead space, and eliminates apparatus (*e.g.* CO_2 absorber, charcoal trap) which can become contaminated.

IMAGING PROCEDURE

The patient is seated with his back to the gamma camera (Fig. 1), breathes in room air and breathes out

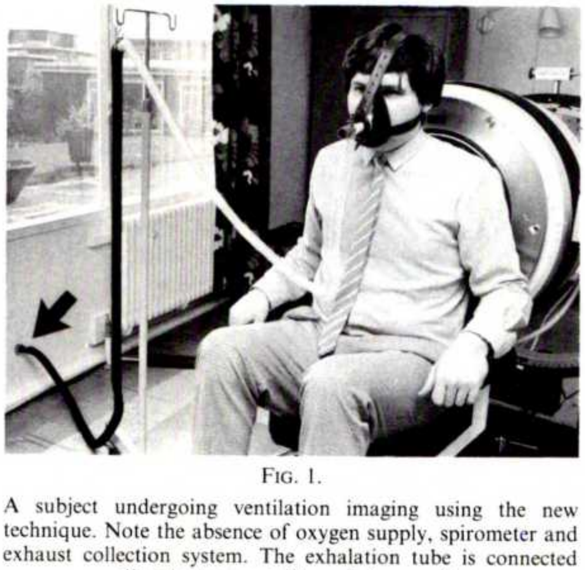

FIG. 1.

A subject undergoing ventilation imaging using the new technique. Note the absence of oxygen supply, spirometer and exhaust collection system. The exhalation tube is connected directly to an outside wall (arrowed).

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*Author for correspondence.

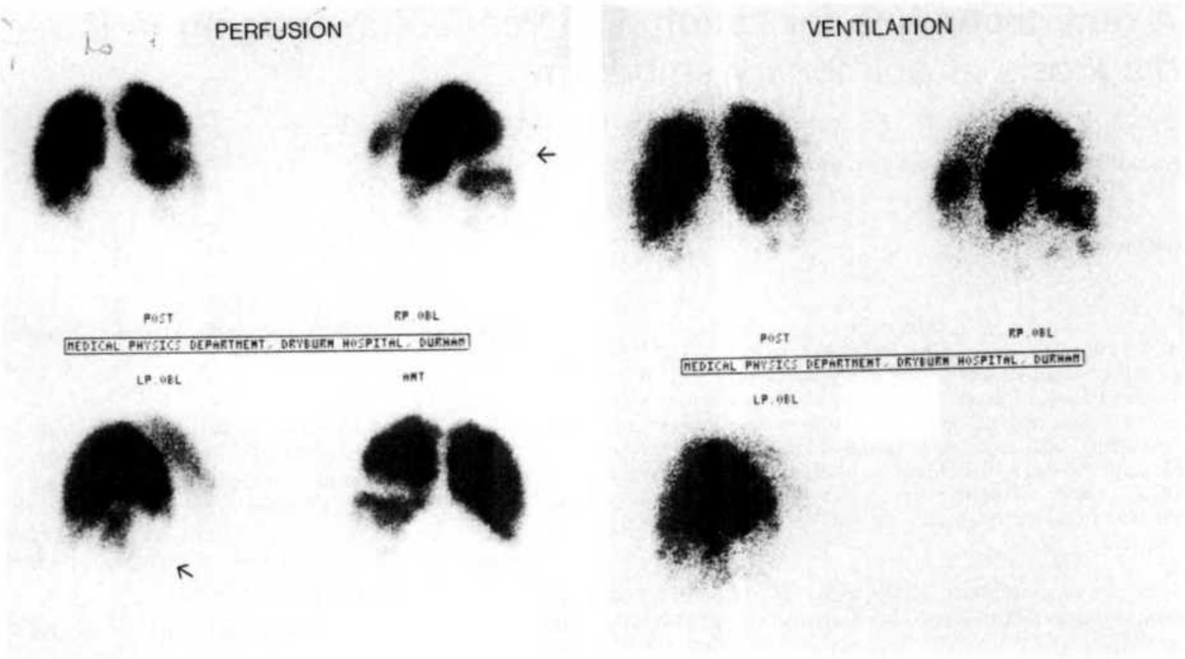
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FIG. 2.

A V/Q scan in a 60-year-old woman with chronic lung disease and suspected pulmonary embolism. The scan does not support embolic disease.

through a tube connected directly to the outside. He completes a tidal exhalation. During the inhalation to vital capacity, 200 MBq of ^{133}Xe is injected into the mouthpiece. The patient holds his breath for 15–20 s, and during this period an image containing 140–180 kcounts is obtained. The patient then exhales and quickly washes out the xenon to the outside air. The patient is encouraged to breathe deeply and rapidly to wash out as quickly as possible. The patient is then repositioned in the right posterior oblique (RPO) projection and the procedure repeated. Finally, the procedure is repeated again in the left posterior oblique (LPO) projection. The total investigation time is about 8 min and requires a total activity of 600 MBq.

Figure 2 shows a V/Q scan in a subject with chronic obstructive airways disease (COAD) who was referred for a lung scan to determine the possible presence of associated pulmonary embolism. Although there is good correspondence between the V/Q defects on the posterior projection of both the perfusion scan and the ventilation scan (conventionally the only projection with ventilation imaging using xenon), there are additional (arrowed) perfusion defects seen on both posterior oblique views which we cannot be sure, from the posterior ventilation view alone, are also matched by corresponding ventilation defects. This leaves some doubt as to whether PE is, in fact, present. However, inspection of the two posterior oblique ventilation views shows clearly that these perfusion defects have corresponding ventilation defects which makes the diagnosis of PE much less likely on the appearance of the scan alone.

The V/Q scan of a patient with a similar problem, that is, the possibility of PE in the presence of COAD, is illustrated in Fig. 3. Inspection of the perfusion posterior oblique views indicates defects which are clearly not matched on the corresponding ventilation views, supporting the presence of embolic disease. Although it could be argued that this conclusion could have been reached from the posterior ventilation view alone, there is little doubt that the two oblique ventilation views strongly reinforce the diagnosis of PE.

VALIDATION OF THE TECHNIQUE

Fifty-two perfusion lung scans containing at least one defect were presented to two experienced observers who were each asked to record the number of independent perfusion defects seen in the four projections: antero-posterior (AP), postero-anterior (PA), RPO and LPO. After viewing each perfusion scan, each observer was shown the inhalation image in the PA projection only and asked to record the number of ventilation defects that corresponded to perfusion defects. Finally, each observer viewed all three inhalation views (PA, RPO and LPO) and again recorded the number of independent, matched ventilation defects. The results are summarised in Table I, where it may be seen that viewing all three inhalation projections significantly

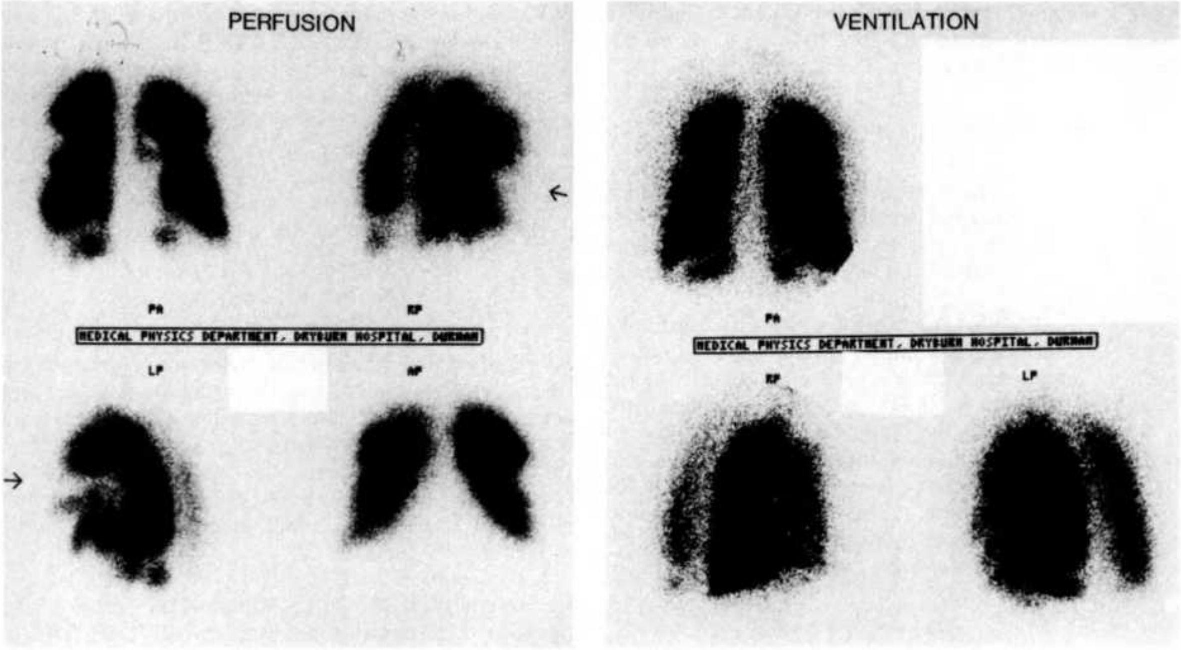

FIG. 3.

A V/Q scan in a 73-year-old man with chronic lung disease and suspected pulmonary embolism. The scan is indicative of embolic disease.

increased ($p < 0.05$) the ability to match V/Q defects. Furthermore, there was no significant difference between the two observers in their estimate of matched and non-matched perfusion defects.

DOSIMETRY

Despite the relatively large amounts of activity used in our procedure, the estimated radiation dose to the patient is similar to that delivered by existing methods. Calculations of radiation dose from inhaled ^{133}Xe are performed in two stages (Goddard & Ackery, 1975; Atkins et al, 1980). Firstly, the time variation of activity in the lungs and other source organs is modelled using empirical observations and assumptions. Secondly, the absorbed dose to the target organs is calculated, either using the standard MIRD scheme (Snyder et al, 1975), or using more detailed models for local energy deposition (Goddard & Ackery, 1975; Lassen, 1984). Our procedure can be adequately compared with existing techniques by performing only the first stage of these calculations. If the activity in the lungs is $A(t)$ Bq, then the area under the time–activity curve is:

$$\bar{A} = \int_0^{\infty} A(t)\, \mathrm{d}t \qquad (1)$$

Using SI units, $\bar{A}$ is a dimensionless number, and will be proportional to the actual radiation dose received by the lungs for almost all dosimetric models. Values of $\bar{A}$ may, therefore, be used to compare relative doses received using different techniques for administration of ^{133}Xe. Three techniques will be compared.

(a) Washin/washout

The patient re-breathes a mixture of ^{133}Xe and oxygen from a closed spirometer for several minutes. After the equilibrium image has been obtained the activity is washed out from the lungs using room air (Goddard & Ackery, 1975; Alderson et al, 1976). Let the mean lung volume be V ml and the re-breathing time be t_e s. Then if the spirometer concentration C Bq

TABLE I

THE NUMBER OF SCANS IN WHICH OBSERVERS REGARDED ALL PERFUSION DEFECTS AS MATCHED BY CORRESPONDING VENTILATION DEFECTS ($V = Q$), AND THOSE IN WHICH AT LEAST ONE UNMATCHED PERFUSION DEFECT WAS SEEN ($V < Q$)

Projection on ventilation scan	Number of scans	
	$V = Q$	$V < Q$
Observer A		
PA only	19	32
PA, LPO, RPO	31	21
Observer B		
PA only	14	38
PA, LPO, RPO	26	26

χ^2 test: $p < 0.05$.

ml^{-1} remains approximately constant, and the washin/washout of each area of lung is monoexponential, it can be shown (Goddard & Ackery, 1975) that:

$$\bar{A} = VCt_e \qquad (2)$$

(b) Inhalation, equilibrium and washout

The patient inhales a bolus of ^{133}Xe gas and holds his breath for a short period. The patient then exhales into a spirometer containing oxygen and re-breathes for several minutes.

After the equilibrium image has been obtained the activity is washed out using room air (Alderson et al, 1980; Neumann et al, 1980; Carter et al, 1982). Let the initial lung activity be A Bq, with breath-holding time t_h s. Subsequently, the lung activity falls monoexponentially with rate constant k s^{-1} to a fraction f of its original value as the patient equilibrates with the spirometer (Atkins et al, 1980). Finally, the washout may also be described monoexponentially with rate constant n s^{-1}, commencing t_e s after the study began. The value of $\bar{A}$ is then:

$$\bar{A} = At_h + fA(t_e - t_h) + \frac{(A - fA)}{k} + \frac{fA}{n} \qquad (3)$$

where it is assumed that k is sufficiently large for equilibrium to be reached before washout commences.

(c) Inhalation only

Three separate inhalation studies are performed, with breath-holding t_h s and total administered activity A Bq (*i e* $A/3$ Bq per inhalation). We have found that washout of inhaled activity when no re-breathing has occurred cannot be described by a single exponential At least half of the inhaled activity is cleared more rapidly, with half-clearance time (mean ±1 sd) of 12.3 ± 4.5 s. Assume that the activity is cleared by two equal components with rate constants r and n s^{-1}. The value of $\bar{A}$ is then:

$$\bar{A} = At_h + A/2\ (1/r + 1/n) \qquad (4)$$

TABLE II

VALUES FOR PARAMETERS USED TO ESTIMATE RELATIVE DOSES

Parameter	Value	Reference
V	2500 ml	Atkins et al, 1980
C	$A/5000$ Bq ml^{-1}	Initial activity in a 5 l spirometer
t_e	240 s	Range 180–300 s; Neumann et al, 1980, Goddard et al, 1975
t_h	20 s	
f	0.3	Depends on spirometer volume
k	0.03 s^{-1}	Personal observations, Atkins et al, 1980
n	0.02 s^{-1}	Goddard & Ackery, 1975
r	0 06 s^{-1}	Personal observations

Values for the parameters used in Equations 2, 3 and 4 are shown in Table II, with references where appropriate. Time–activity curves for the three techniques are shown in Fig. 4, accurately drawn using the quoted parameter values and scaled to give equal areas under each curve. These curves, therefore, indicate the relative amounts of activity in the lungs achieved using the three techniques for the same radiation dose.

Calculated values of $\bar{A}$ for the three techniques are:

$$\begin{aligned} &\text{Method (a) } \bar{A} = 120A \\ &\text{Method (b) } \bar{A} = 124A \\ &\text{Method (c) } \bar{A} = \ \ 53A \end{aligned} \qquad (5)$$

As expected, the inhalation-only technique proposed in this paper gives significantly less radiation dose per unit activity. Figures for actual activities administered are not readily available. American groups using Method (b) report activities in the range 370–740 MBq (Alderson et al, 1980; Alderson & Line, 1980; Neumann et al, 1980; Carter et al, 1982), giving values of $\bar{A}$ in the range $4\,6 \times 10^{10}$ to 9.2×10^{10}.

In a recent UK survey, 65 hospitals reported using a mean activity of 240 MBq, although no details of the methods of administration were given (R. A. Shields, personal communication). Assuming that most centres

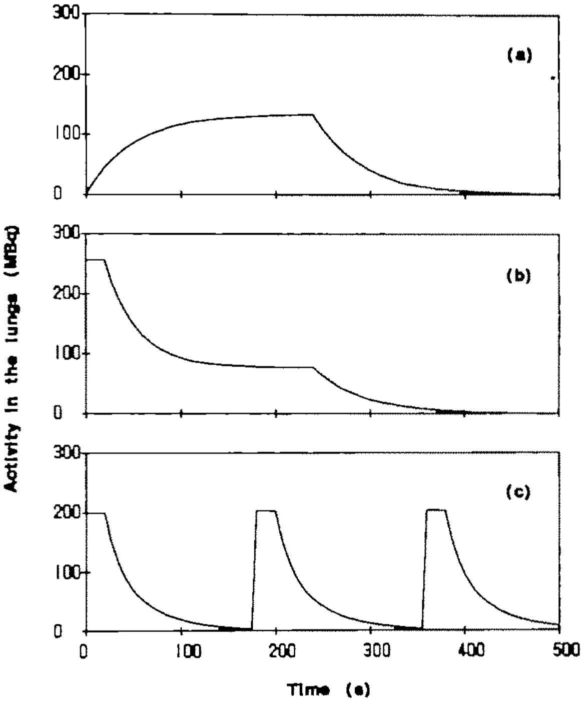

FIG. 4.

Time–activity curves for (a) washin/washout, (b) inhalation, equilibrium and washout, and (c) inhalation-only techniques The curves have been normalised to the same area ($\bar{A} = 3.2 \times 10^{10}$) and, therefore, show the relative lung activity for the same radiation dose.

were using Method (b), then a typical value for $\tilde{A}$ in the UK would be 3×10^{10}. For our proposed technique the same area under the time–activity curve is achieved using a total of 600 MBq ($\tilde{A} = 3.2 \times 10^{10}$).

Discussion

The technique described here provides good-quality images of regional ventilation in three different projections. In this respect it offers the advantages of ^{81}Kr^{m} imaging but does not suffer from the drawback of limited availability; ^{133}Xe is always available for a 24 h, 7-day emergency service, and the whole procedure takes less than 10 min. Also, the first-breath xenon image is purely ventilation-dependent, unlike those images obtained with ^{81}Kr^{m}, which are influenced to a varying extent by both ventilation and lung volume, particularly in patients with PE, who are often tachypnoeic (Nimmo et al, 1986). Whether or not multiple ventilation projections increase diagnostic accuracy remains uncertain. Our objective assessment suggests that it does and this contention is supported strongly by Lavender and Finn (1986), although others remain unconvinced (Nimmo et al, 1986).

The three-view inhalation study advocated above does not permit a study of lung volume and air-trapping which can be obtained from the conventional equilibrium and washout phases, principally because of dosimetric considerations. However, these phases are mainly of value in the assessment of chronic lung disease, which is usually already well known to the referring clinician. Our method concentrates on the only common indication for lung scintigraphy, that is, the acute detection of pulmonary embolism (Nimmo et al, 1986), and in that respect it is the inhalation views which are of most value Alderson et al (1980) compared the ^{133}Xe single-projection inhalation view with washout ventilation imaging as an aid in the diagnosis of pulmonary emboli, and concluded that, to maximise the specificity of ^{133}Xe imaging, a long washout phase should be used. It should be pointed out, however, that in their study only a single-projection inhalation view was obtained and the count density was about 30% of that in each of our three inhalation projections. The same conclusions need not necessarily apply when three inhalation views are available.

The use of ^{99}Tc^{m}-DTPA aerosol ventilation scintigraphy as an alternative to radioactive gases in the diagnosis of pulmonary embolism has been advocated by Buxton-Thomas and Wraight (1984) The main drawback of ^{133}Xe imaging was said to be that only one view of the lungs could be obtained; a statement with which we disagree. However, radioaerosol imaging is not without its limitations: high activities (> 1000 MBq) of ^{99}Tc^{m} are needed to prime the nebuliser; it is necessary to wait about 1 h to allow blood clearance of the inhaled ^{99}Tc^{m} aerosol before the ^{99}Tc^{m} perfusion scan is begun (Buxton-Thomas & Wraight, 1984); radioaerosol examinations are more likely to be technically unsatisfactory than those using radioactive gases (Alderson et al, 1984); and the additional technical complexities of aerosol imaging make it less acceptable than radioactive gases for an out-of-hours service (Nimmo et al, 1986).

Acknowledgment

We are grateful to Dr N T A. Couper for his helpful interest in this work.

REFERENCES

Alderson, P O , Biello, D. R., Gottschalk, A , Hoffer, P. B , Kroop, S. A , Lee, M E., Ramanna, L., Siegel, B. A. & Waxman, A. D., 1984 Tc-99m-DTPA aerosol and radioactive gases compared as adjuncts to perfusion scintigraphy in patients with suspected pulmonary embolism *Radiology, 153,* 515–521.

Alderson, P. O., Biello, D R., Khan, A R., Barth, K. H., McKnight, R C. & Siegel, B. A., 1980. Comparison of ^{133}Xe single-breath and washout imaging in the scintigraphic diagnosis of pulmonary embolism. *Radiology, 137,* 481–486.

Alderson, P O & Line, B R., 1980 Scintigraphic evaluation of regional pulmonary ventilation *Seminars in Nuclear Medicine, X(3),* 218–242.

Alderson, P O., Rujanavech, N , Secker-Walker, R. H. & McKnight, R. C , 1976 The role of ^{133}Xe ventilation studies in the scintigraphic detection of pulmonary embolism. *Radiology, 120,* 633–640

Atkins, H L , Robertson, J. S , Croft, B. Y., Tsui, B., Susskind, H., Ellis, K J , Loken, M K & Treves, S., 1980 Estimates of radiation absorbed doses from radioxenons in lung imaging (MIRD Report No. 9). *Journal of Nuclear Medicine, 21,* 459–465.

Blinder, R. A. & Coleman, R. E., 1985 Evaluation of pulmonary embolism *Radiologic Clinics of North America, 23,* 391–405

Buxton-Thomas, M. S & Wraight, E P., 1984 The use of ^{99}Tc^{m}-DTPA aerosol ventilation scintigraphy in the diagnosis of pulmonary embolism. *Nuclear Medicine Communications, 5,* 387–391.

Carter, W D , Brady, T. M , Keyes Jr, J W., Thrall, J. H , Greenhouse, J. B., Biello, D R., Siegel, B A., Alderson, P. O & Brady, T. J , 1982 Relative accuracy of two diagnostic schemes for the detection of pulmonary embolism by ventilation-perfusion scintigraphy. *Radiology, 145,* 447–451.

Goddard, B. A & Ackery, D. M., 1975 Xe-133, Xe-127 and Xe-125 for lung function investigations a dosimetric comparison *Journal of Nuclear Medicine, 16,* 780–786

Lassen, N A , 1984. Assessment of tissue radiation dose in clinical use of inert gases, with examples of absorbed doses from ^{3}H, ^{85}Kr and ^{133}Xe. *Minerva Nucleare, 8,* 211–217.

Lavender, J. P. & Finn, J P., 1986. Economics of xenon 127, xenon 133 and krypton 81m for routine ventilation imaging of the lungs (letter). *British Journal of Radiology, 59,* 298.

McNeil, B. J , 1976. A diagnostic strategy using ventilation-perfusion studies in patients suspect for pulmonary embolism *Journal of Nuclear Medicine, 17,* 613–616.

Neumann, R D , Sostman, H. D. & Gottschalk, A , 1980 Current status of ventilation-perfusion imaging. *Seminars in Nuclear Medicine, X(3),* 198–217

Nimmo, M J., Merrick, M V & Millar, A. M , 1986. Economics of xenon 127, xenon 133 and krypton 81m for routine ventilation imaging of the lungs (letter) *British Journal of Radiology*, *59*, 298–299.

Snyder, W. S., Ford, M R., Warner, G. G. & Watson, S. B., 1975. *"S", Absorbed Dose per Unit Cumulated Activity for Selected Radionuclides and Organs*. MIRD Pamphlet No. 11 (Society of Nuclear Medicine, New York)

Book reviews

Radiopharmacy and Radiopharmaceuticals. Ed. by A. E Theobald, pp. xii + 203 + index, 1985 (Taylor and Francis Ltd, London), £22.00.
ISBN 0–85066–318–0

This book is the compilation of the texts given at a short course at Chelsea College in 1983 The speakers have somewhat extended and updated their papers and, as such, the book falls into two main sections comprising recent developments in radiopharmaceuticals and contemporary radiopharmacy practice Six topics from each section are included, and, as well as discussing state-of-the-art work, each topic is introduced with a comprehensive and well referenced history.

Radiopharmaceuticals discussed are those suitable for lung ventilation, immunoscintigraphy, cell labelling, gastric studies, new generator systems and iodine ^{123}I products These pharmaceuticals, being non-technetium based, present greater problems for their production and the neatly overlapping second section discusses the design, control and monitoring of the radiopharmacy necessary to produce them. Radiation protection is well covered, although all these topics were written before *The Ionising Radiations Regulations 1985* and associated *Approved Code of Practice*. However, this does not detract from the advice given in the text.

Finally, chapters on radiopharmaceuticals for therapy and the altered uptake of radiopharmaceuticals as a result of drug/non-drug interaction round off a book which is likely to be of interest to all members of radionuclide diagnostic departments, especially those considering diversifying into routine non-technetium based scintigraphy. It provides well presented, detailed information on production techniques for these radiopharmaceuticals and the facilities required, bearing in mind the current philosophy of the Medicines Inspectorate

The book is good value and will be a useful addition to all departmental libraries

P J Maltby

Sensitivity and Specificity of Common Scintigraphic Procedures. a review of clinical efficacy. By Michael L. Goris, pp x + 119 + index, 1985 (Blackwell Scientific Publications, Oxford), £28 50
ISBN 0–8151–38091

When this book first arrived on my desk for review I was enthusiastic about the title, in particular the subtitle, *A review of clinical efficacy*, because I believe this is an important area of diagnostic medicine that has been relatively ignored· unfortunately, it is not about efficacy

As I read I found myself progressively disappointed, because it is a patchy book which is often difficult to read, containing tables that are difficult to follow, and is far from being comprehensive, only a few radionuclide procedures are included. The feeling one has from reading it is that the author became rather bored with the whole project half way through and decided to publish as it was, rather than complete it, presumably this was in about 1983, as there are no references later than this. This is regrettable as there are many important contributions to sensitivity, specificity and efficacy that have appeared subsequently and, presumably, could have been included at a later stage.

All in all, this is not a book that I can recommend; certainly it is not suitable for the clinician, whom the author in his introduction indicates as his potential primary audience No clinician would want a book devoted to only a few tests in one imaging modality when the major problem is deciding between several. It may, however, prove to be a useful reference to be aware of, when one wishes to look up a sensitivity or specificity for a particular investigation; but because of the lack of complete coverage, Murphy's law will almost certainly apply and the one you want will not be included. Finally, I was intrigued to know who Dr Josiane Bretille, M.D., is. she has apparently co-authored half of the chapters in this book but gets no mention in the credits, I think we should be told

M N. Maisey

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Bone scintigraphy in lung cancer: a reappraisal

By M. V. Merrick and J. M. Merrick

Department of Nuclear Medicine, Western General Hospital, Edinburgh EH4 2XU

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ABSTRACT

The prognostic significance of bone scintigraphy was investigated by following 587 consecutive patients with lung cancer, in whom this investigation had been performed, for up to 9 years, or until death. Survival was unrelated to age, sex or cell type. However, pain and abnormal bone scintigraphy were both independently associated with a significantly reduced survival compared with those who were free of pain or who had normal bone scintigraphy. These factors were cumulative. The association remained equally valid for all cell types. Claims that a single metastasis is not prognostically significant are unfounded. It is suggested that the results of some chemotherapy trials must be reconsidered in the light of present findings, because of the lack of adequate control groups; the results could be construed to show a beneficial effect only in patients with bone metastases and a poor prognosis, but little or no effect in patients with normal bone scintigraphy. As judged by clinical and radiological follow-up and post-mortem examination, skeletal scintigraphy in patients with lung cancer had a sensitivity of 0.89, a non-specificity (false positives/true negatives) of 0.00 and an accuracy of 0.78. With existing radiopharmaceuticals there is an irreducible residue of false negatives due to deposits which provoke little or no osteoblastic response. Bone scintigraphy is, thus, indicated in any patient with lung cancer with unexplained symptoms and whenever staging is required, because of the prognostic implications. It should precede other staging investigations because the high detection rate may render other tests unnecessary.

Lung cancer remains a major cause of morbidity. Between 1971 and 1980 the crude prevalence in Scotland increased from 23 to 43 per 100 000 per annum (Scottish Cancer Registry, 1984). The prognosis is poor, survival being shorter for patients with small-cell tumours than for other histological types (Festenstein & Weatherstone, 1985). Even with intensive chemotherapy, only 13% of those with limited and 2% of those with widespread small-cell tumours survived for 2 years (Morstyn et al, 1984).

Detailed staging is not indicated when the disease is so advanced at presentation that palliative treatment alone is appropriate, but should be reserved for patients being considered for radical therapy (McNeil et al, 1977). There are several recognised systems (Roswit et al, 1968; American Joint Committee for Cancer Staging and End Result Reporting, 1973, Little et al, 1983), but none is as widely employed as are the equivalent schemas for other common tumours, because of reservations about both their accuracy (Matthews et al, 1973) and their usefulness (Ihde et al, 1981). However, it has been suggested that stage is prognostically more important than the histological classification (Little et al, 1983; Spiro, 1985).

Bone is one of the commonest sites for early extrathoracic spread (Komaki et al, 1977; Kelly et al, 1979; Ihde et al, 1981) but, despite the obvious attraction of skeletal scintigraphy as a staging investigation, there have been no comprehensive studies of its prognostic significance in relation to symptoms, cell type or biochemical markers, there are deficiencies in the few published correlations between scintigraphy and post-mortem findings. Advances in chemotherapy have been associated with improvements in both the duration and the quality of survival. With the high cost, widening choice, increasing effectiveness and greater specificity of available therapeutic regimes, there is a need for better information about the reliability of available methods of determining the extent of disease.

We report here an analysis of 587 consecutive patients with proven carcinoma of the lung, referred for bone scintigraphy between 1975 and 1982 and followed for up to 9 years, or until death. Post-mortem examinations were carried out in almost 10%. The termination of this series coincided with the initiation of systematic trials of chemotherapy. The results, therefore, reflect the natural history of the various histological forms of lung cancer unmodified by effective systemic therapy.

PATIENTS AND METHODS

Between January 1975 and December 1982, 5300 consecutive patients referred for skeletal scintigraphy were entered into a prospective study. In 1983 the departmental records were reviewed and notes obtained from the referring hospital or unit. Initially, 627 were identified from either the departmental records or the clinical notes as having a possible or probable diagnosis of carcinoma of the bronchus. Forty were subsequently excluded either because their notes could not be traced or because lung cancer had not been confirmed, leaving 587 in whom the diagnosis had been confirmed histologically or the radiographic and clinical findings were such as to leave no reasonable doubt.

Indications for referral could be grouped into three major categories:

(1) investigation with a view to subsequent radical surgery or radiotherapy,

(2) a proven tumour and symptoms suggestive of

metastases, often with normal or equivocal radiographs, and

(3) patients without any known primary, most commonly being investigated for back pain, but subsequently proven to have a bronchogenic cancer.

These distinctions were not exclusive. There was some overlap and it was not possible to categorise the reason for referral unambiguously in many cases. It was accepted practice in all the referring units that patients were fully investigated before radical treatment. Scintigraphy was usually one of the first investigations to be performed, but was omitted if disease was obviously advanced, when the findings could not influence management. Because of local factors, few if any patients with lung cancer were referred during the period of the study to the only other hospital in the area with radionuclide imaging facilities. The series thus includes virtually all patients with lung cancer requiring scintigraphy for staging or other reasons. The number of patients investigated was approximately one quarter of the number of cases of lung cancer reported to the local cancer registry during this period.

Dates of birth, diagnosis, imaging, death or last attendance, sex, histology, scintigraphic and radiographic findings, subsequent course, symptomatology, alkaline phosphatase levels and any other available relevant information were recorded. Copies of post-mortem reports were obtained from the Department of Pathology if not filed in the notes. Post-mortem examination was performed whenever possible. In practice, it was possible only when patients died in hospital. This was determined by clinical and social factors: wherever possible, patients were allowed to die at home. Patients were, thus, nominally unselected, but it is not possible to determine whether these patients were typical of the whole. The same objection applies to all post-mortem series. The referring units did not routinely perform TNM staging of lung tumours during this period.

Until 1977, scintigraphy was performed with an Ohio Nuclear series 100 gamma camera fitted with a whole-body scanning attachment. Subsequently, a Cleon 760 multidetector scanner was used. Examinations were carried out 2–5 h after intravenous administration of 700 MBq (20 mCi) of $^{99}Tc^{m}$ MDP. Settings were adjusted to give a count density sufficient to maximise the detection of both photon-rich and photon-deficient lesions (Merrick, 1973, 1984). All the studies were reported or reviewed (with radiographs of all suspect regions) by M.V.M. The radiographs were subsequently seen by at least three independent observers: a consultant radiologist, a radiotherapist and a chest physician or surgeon. Any divergence of interpretation was resolved by consensus.

The complete series was re-examined in 1984/85, initially without knowledge of the original reports. All of the scintigrams, but few of the radiographs, were still available, so that interpretation of the significance of any abnormality usually rested upon the contemporary consensus interpretation of the radiographs. For the purpose of this review, studies were classified as normal if there was no scintigraphic abnormality or if there was a definite benign explanation for the scintigraphic findings (osteoarthritis, osteomalacia, etc.). They were regarded as abnormal only if there was radiographic confirmation of at least one metastic site. The remaining cases, including those in whom adequate radiographs were not available and those with scintigraphic abnormalities for which there was neither a benign nor a malignant explanation, were classified as equivocal, even though originally reported as "suggestive of" or "probable" deposits.

Survivals were compared using the Lee Desu variant of the log-rank test. Groups were compared using standard χ^2 tests, with corrections where appropriate.

RESULTS

The age range of the population studied is shown in Fig. 1 and the distribution of histological types in Table I. Table II summarises the relationship between histology and scintigraphic findings in patients imaged within 8 weeks of diagnosis compared with that in patients imaged at later times. There was no significant difference in the prevalence of deposits in any category between subjects imaged early and those imaged late. There were minor discrepancies in the number of affected sites, but no case would have had its classification altered significantly as a result of the review at the end of the study.

The relationship between age, sex and scintigraphic findings is detailed in Tables III and IV. Many of the subgroups are rather small. The differences between the prevalence of metastases in different histological types and between males and females are not statistically significant. Survival from time of diagnosis of patients who did not have skeletal metastases was significantly longer than of those with deposits, for all histological types (Table V and Figs 2, 3).

Three hundred and sixty-four patients (62%) had complained of pain by the time scintigraphy was performed. Of those with pain, 60% had scintigraphic evidence of skeletal metastases and a further 13% had

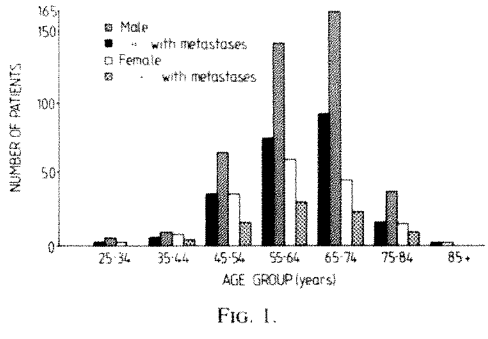

FIG. 1.

Age distribution of the population studied.

TABLE I

Types of tumour

Histology	No. of patients		% of total with this histology	% of type with significant abnormality*
	Male	Female		
Oat cell	97	45	24	49
Squamous	143	45	32	50
Adenocarcinoma	32	14	8	63
Mixed or undifferentiated	19	11	5	37
Large cell	25	12	6	57
No histology	102	36	24	55
Mesothelioma	5	1	1	33

*χ = 7.54, 6 d.f., (not significant)

scintigraphic evidence of degenerative or other benign bone disease. The pain was considered to be of extraskeletal origin or remained unexplained in the remainder. The survival of patients complaining of pain at diagnosis was shorter than of those without ($\chi^2 = 14.64$; 1 d.f.; $p < 0.001$).

The alkaline phosphatase level was recorded as elevated in 68 patients (12%). It was, however, the policy in some units not to preserve normal laboratory results. This figure is therefore a minimum estimate, as it was not possible to distinguish between a normal result, failure to incorporate an abnormal result into the notes and non-performance of the test.

Post-mortem examinations were obtained in 57 (9.7%) of the patients, 40 males and 17 females (Table VI) Because it was possible to obtain a post-mortem examination only when patients died in hospital, the survival figures of this group are weighted by a small number who were admitted undiagnosed and had a short, terminal illness. There were seven false negatives and no false positives in cases with a non-equivocal report Skeletal metastases were found in three of the eight equivocal cases. One patient who died 3 years after normal scintigraphy had no skeletal metastases post-mortem, nor were any suspected clinically This was considered a true negative. In the remainder, the median interval between scintigraphy and death was 33 (range 1–297) days; 85% had died within 90 days. The mean age at death was 61.8 years (range 28–80 years, SD10 years). not significantly different from that of the whole series.

Discussion

The range of reported prevalence of skeletal metastases in carcinoma of the bronchus (Table VII) is too large to be dismissed as statistical fluctuations. There is no reason to assume that any published series consists either of a representative or of a randomly selected sample of the full population. In all series there was clearly selection of patients in one form or another In most, neither the criteria for inclusion nor the composition of the original population are defined. Our population consisted of all patients residing in the south-east of Scotland with lung cancer in whom skeletal scintigraphy was considered clinically relevant by the responsible clinician.

Older post-mortem series (Gilbert & Kagan, 1976; Komaki et al, 1977), pre-dating the introduction of antibiotics, variously put the prevalence of skeletal metastases as between 14% and 50%, but did not distinguish between cell types More recent series (Abrams et al, 1959; Auberbach et al, 1975; Matthews,

TABLE II

Effect of delay on scintigraphic findings

Histology	Interval between diagnosis and first bone scintigraphy			
	Less than 8 weeks		More than 8 weeks	
	Total no.	Abnormal (%)	Total no	Abnormal (%)
Oat cell	74	50	68	51
Squamous	83	47	105	52
Adenocarcinoma	14	64	32	63
Large cell	21	48	16	69

TABLE III

AGE DISTRIBUTION OF METASTASES IN MALES

Histology	Age 25–54 years		Age 55–74 years		Age ≥75 years	
	Total no	Abnormal (%)	Total no	Abnormal (%)	Total no	Abnormal (%)
Oat cell	25	14 (56)	65	29 (45)	7	4 (57)
Squamous	19	10 (53)	113	58 (51)	11	7 (64)
Adenocarcinoma	8	6 (75)	23	15 (65)	1	0
Mixed or undifferentiated	8	5 (63)	9	6 (67)	2	1 (50)
Large cell	4	2 (50)	20	14 (70)	1	0
No histology	13	5 (38)	74	44 (59)	15	6 (40)

1976) have found a prevalence in the upper part of this range. As Matthews (1976) showed, routine post-mortem examinations often do not include an exhaustive examination of the skeleton and, thus, underestimate the true prevalence of bone metastases by a substantial amount. These figures, therefore, represent a minimum estimate of the true prevalence and, as Kies et al (1978) pointed out, probably account for the high "false positive" rate of bone scintigraphy in some series, including their own.

Scintigraphic series make no pretence of being a random cross-section. Patients are referred because the test is expected to yield clinically useful information. Most report a rather lower prevalence than the post-mortem series, although that in the present series was 310 out of 587 (53%). Factors, not mutually exclusive, contributing to this variation include differing perceptions of the indications for investigation, the criteria of defining abnormality and the completeness of both post-mortem and scintigraphic examinations. The additional possibility of real differences between populations cannot be excluded. Moreover, when investigations for conditions such as metastases are performed sequentially, the detection rate of any one investigation will depend on its order in the sequence. In our series, skeletal scintigraphy was one of the earlier tests to be performed, one department serving both the primary population and the secondary referral centre.

Small-cell tumours

Less information is available about the variation of prevalence with cell type (Table VIII). Hansen and Muggia (1972) obtained positive iliac-crest biopsies in 46% of patients with small-cell carcinomas. A more recent series (Ohnoshi et al, 1982) reported less than half this frequency Auerbach et al (1975) found bone metastases post-mortem in 35% of 163 patients, while Matthews (1976) observed a prevalence of 37% in her "retrospective" series but 55% overall prospectively It was higher still in patients with less differentiated tumours (Matthews & Gazdar, 1981).

The figure of 49% in patients with small-cell tumours in the present series was slightly higher than in most other scintigraphic studies (Table VIII). This discrepancy must be seen in the context that Levenson et al (1981) and Ihde et al (1981) apparently include common material, while their scintigraphic technique is not fully described. As far as can be ascertained, they employed low count-density images, which have been shown to underestimate the true prevalence of deposits (Merrick, 1973). The lower prevalence found by Dimmler and Nachbur (1984) is probably due to pre-

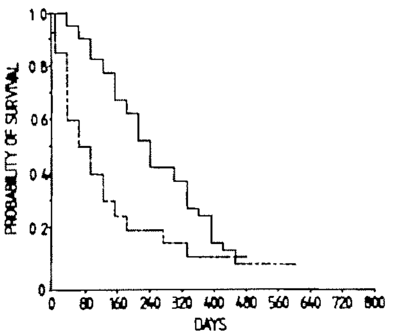

FIG. 2

Actuarial survival of patients with squamous carcinoma of bronchus Solid line = scintigraphy normal; broken line = scintigraphy abnormal; $\chi^2 = 16.97$; 1 d f.; $p < 0.001$

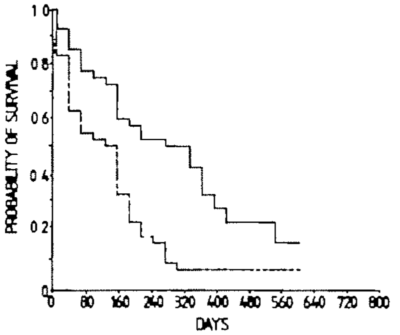

FIG. 3.

Actuarial survival of patients with oat-cell carcinoma of bronchus Solid line = scintigraphy normal; broken line = scintigraphy abnormal, $\chi^2 = 8.94$, 1 d.f.; $p < 0.01$

TABLE IV

Age distribution of metastases in females

Histology	Age 25–54 years		Age 55–74 years		Age ≥ 75 years	
	Total no	Abnormal (%)	Total no.	Abnormal (%)	Total no	Abnormal (%)
Oat cell	16	5 (31)	26	16 (62)	3	2 (67)
Squamous	8	2 (25)	34	16 (47)	3	1 (33)
Adenocarcinoma	7	4 (57)	5	3 (60)	2	1 (50)
Mixed or undifferentiated	2	2 (100)	8	4 (50)	1	0
Large cell	4	2 (50)	7	3 (43)	0	0
No histology	6	4 (66)	24	12 (50)	6	5 (83)

selection of patients referred to a thoracic surgical clinic. As we accepted only cases in which there was radiological confirmation of metastases and as the diagnosis was confirmed in all examined post-mortem, the higher figure is unlikely to be incorrect in our population. The prevalence was similar, irrespective of whether patients were imaged at presentation or late in the course of the disease (Table II), suggesting that in many cases metastasis to bone preceded the event directing the patient to medical attention.

Squamous carcinoma

Similar considerations apply with squamous carcinoma, in which the difference between the present and previous series is much greater. The post-mortem prevalence has been reported as 25 6% of 233 (Auerbach et al, 1975), 20% of 126 (Matthews, 1976, retrospective) or 23% of 35 (*ibidem*, prospective). The low prevalence found scintigraphically by Napoli et al (1973) may be the result of limitations imposed by their employment of strontium isotopes. The difference between that reported by Dimmler and Nachbur (1984) and ourselves is likely, as with small-cell tumours, to be related to criteria of selection of patients referred for examination, theirs apparently being considered for surgery, while ours includes a substantial number investigated before referral to a surgical clinic, in whom there was a clinical suspicion of metastases Because of the way in which our patients were referred, these two groups cannot be reliably separated. However, in view of the confirmation in all of our patients examined post-mortem and the stringency of the criteria defining abnormality in the others, there can be no doubt that the prevalence of skeletal metastases in patients referred to us for skeletal scintigraphy was high. It is arguable that this figure may be more representative of the population needing investigation

Other cell types

The highest prevalence is found in adenocarcinoma. Our population (30/46) was similar in this respect to the only previous large scintigraphic series (Oyamada et al, 1978), but showed a higher prevalence than Matthews' "prospective" (15/33) or either retrospective post-mortem series (40/110, 73/167) We did not corroborate Oyamada's finding of a much lower figure in patients imaged within 8 weeks of diagnosis, nor were we able to test Matthews' observation of a higher prevalence in patients with less differentiated tumours. It is noteworthy that Dimmler and Nachbur (1984) found a lower prevalence in this group also, as well as in large-cell carcinoma. Indeed, the only cell type in which we found a lower prevalence than these authors was undifferentiated carcinomas. The prevalence in our patients with large-cell tumours was similar to that in Matthews' "prospective" post-mortem series, but higher than both of her retrospective post-mortem series

Survival

Gravenstein et al (1979) and Levenson et al (1981) both found abnormal skeletal scintigraphy to be

TABLE V

Mean survival

Histology	Scintigraphy abnormal		Scintigraphy normal	
	Mean age (years)	Mean survival (days)	Mean age (years)	Mean survival (days)
Oat cell*	58 7	148	54.9	245
Squamous*	63 8	128	62 8	282
Adenocarcinoma	57.7	195	54.3	309
Large cell	64 0	108	67 9	225

* Includes only those patients imaged within 8 weeks of diagnosis.

TABLE VI

CORRELATION BETWEEN SCINTIGRAPHIC AND POST-MORTEM FINDINGS

Histology	True positive	True negative	False negative scintigraphy	False negative post-mortem examination	Scintigraphy equivocal
Oat cell	9	3	2		1 post-mortem + 1 post-mortem −
Squamous	8	3	2		1 suspect region not seen post-mortem
Adenocarcinoma	6		1		2 post-mortem −
Mixed or undifferentiated	4	3	2	1	
Large cell	2				1 post-mortem + 2 post-mortem −
Mesothelioma	1	1		1	
Total	30	10	7	2	8

associated with a reduced survival However, the former did not distinguish between histological types, while the latter considered only patients with oat-cell tumours receiving chemotherapy The difference in survival between the two groups in the latter series, although statistically significant, was small. Ihde et al (1981) found that the survival of patients receiving chemotherapy who had deposits limited to a single site was similar to that of patients with local disease. Their text is ambiguous, but it appears that the skeleton was regarded as a single site. They did not analyse the number of involved locations. This has been misquoted in many subsequent papers. Neither of these series assessed survival in patients not receiving chemotherapy. Irrespective of the precise meaning, it is evident that their conclusions were based on data lacking a proper control population.

The substantial prognostic importance of scintigraphic abnormalities in patients not receiving chemotherapy is confirmed in the present series for all major histological categories (Table V and Figs 2, 3). Indeed, the duration of survival of patients without skeletal metastases is approximately double that of those with them. If the findings from the present series can be extrapolated to the earlier ones, it may be concluded that the effect of chemotherapy on survival is much greater in patients with skeletal metastases and a poor prognosis, than in those with more localised disease (which has a better prognosis even if untreated). It may

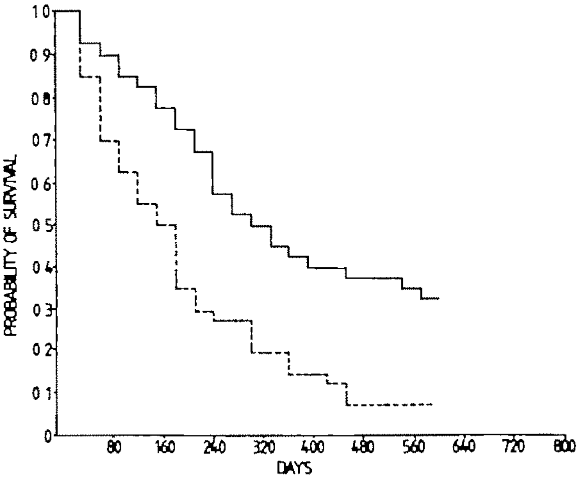

FIG. 4

Actuarial survival of asymptomatic patients with carcinoma of bronchus Solid line = scintigraphy normal, broken line = scintigraphy abnormal, $\chi^2 = 9.82$, 1 d f, $p < 0.01$

TABLE VII

PREVALENCE OF SKELETAL METASTASES IN LUNG CANCER

Authors	Year	No of cases	Prevalence (%)
Napoli et al	1973	110	38 (35)
Scott & Adams	1974	56	12 (21)
Shirazi et al	1974	264	119 (45)
Tofe et al	1975	230	147 (64)
Williams et al	1977	100	37 (37)
Donato et al	1979	60	20 (33)
Gravenstein et al	1979	113	46 (41)
Kelly et al	1979	88	40 (46)
Levenson et al	1981	119	49 (41)
Dimmler & Nachbur	1984	227	53 (23)
Present series	1986	587	310 (53)
Total		1844	833 (45)

$\chi^2 = 115.64$; 10 d f, $p < 0.001$

TABLE VIII

PREVALENCE OF METASTASES BY CELL TYPE

Authors	Year	Small cell	Squamous	Adenocarcinoma	Large cell	Undifferentiated
Napoli et al	1973	11/22 (50%)	9/36 (25%)	8/21 (38%)	10/31 (32%)	
Oyamada et al	1978			64/106 (60%)		
Bitran et al	1981	17/30 (57%)				
Levenson et al	1981	49/119 (41%)				
Ihde et al	1981	40/106 (38%)				
Dimmler & Nachbur	1984	16/37 (38%)	33/105 (31%)	13/27 (48%)	5/17 (29%)	18/41 (44%)
Present series	1986	70/142 (49%)	94/188 (50%)	29/46 (63%)	21/37 (57%)	11/30 (37%)

be questioned whether there was any benefit from treatment of patients with normal scintigraphy. The suggestion that skeletal scintigraphy is not prognostically useful is clearly erroneous.

Maurer and Pajak (1981) reported that the survival of patients with a single skeletal metastasis was no worse than that of patients with normal scintigrams. However, this conclusion was based on only seven cases. The sites of the abnormalities were not stated and in none was there either radiological or other confirmation of the nature of the scintigraphic abnormality. As Corcoran et al (1976) pointed out, at least one third of solitary scintigraphic lesions are benign. The percentage is higher in ribs (Talarico et al, 1982; Tumeh et al, 1985), up to 90%, while interpretation of bone scintigraphy limited to counting "hot spots" can give a false positive rate of 70% or more (Merrick, 1986). The number of patients with solitary deposits in the present series is too small for useful statistical analysis, especially as a number of patients had several scintigraphic abnormalities, only one of which was proven to be a deposit. It is not reasonable to conclude, on the basis of available evidence, that a single skeletal deposit is of no prognostic significance.

Pain

A higher prevalence of bony deposits has been reported in symptomatic than in asymptomatic patients. We found the prevalence of skeletal metastases to be 257 out of 488 (57%) in those with symptoms, similar to that found in some post-mortem series (Gilbert & Kagan, 1976), although lower rates have been reported in patients dying shortly after "curative" resections (Matthews et al, 1973) Kies et al (1978) detected scintigraphic abnormalities in 90% of symptomatic patients, and White et al (1982) identified deposits in the presence of bone pain or tenderness in 22 out of 25 patients (88%), while Hooper et al (1978) and Dimmler and Nachbur (1984) observed that 48% of patients with scintigraphic abnormalities had bone pain. Scott and Adams (1974), on the other hand, found skeletal metastases in only 12 out of 56, all of whom had pain, but none in patients who were asymptomatic, possibly because they were limited to what would now be regarded an inadequate activity of $^{87}\mathrm{Sr}^{m}$.

The various series are not directly comparable, as different definitions of "symptomatic" have been employed, some including only bone pain while others include non-specific pain and symptoms such as weight loss. The prevalence of deposits in patients with pain in the present series was 57%, while 62% of those with evidence of bone metastases were symptomatic. The survival of patients with pain was significantly shorter than that of those without ($\chi^2 = 14.64$; 1 d.f., $p < 0.001$), and abnormal skeletal scintigraphy in addition carried a worse prognosis still. However this group is defined, there is no disagreement that symptomatic patients yield a substantial incidence of clinically and prognostically important scintigraphic abnormalities, many of which are not readily identified by any other technique Scintigraphy is, thus, indicated in any patient with pain for which no explanation is apparent on plain radiographs.

Screening

In comparison with the high detection rate in symptomatic patients, Hooper et al (1978) found abnormalities in only four out of 49 who were asymptomatic, in two of whom deposits were not subsequently confirmed, while Kelly et al (1979) detected them in eight out of 59 (13.6%). Four with definite deposits were detected from a group of 57 patients with operable peripheral tumours (Turner & Haggith, 1981). In three this was due to local rib involvement and did not contraindicate thoracotomy, while the fourth also had liver deposits. Two of five further patients in this series with probably abnormal scintigrams did not develop evidence of skeletal metastases during a follow-up of 28 months and 30 months, respectively, and were, therefore, regarded as false positives. All of these studies can be criticised either because of extrapolation from selected to unselected populations or on technical grounds. Some relied on low count-density surveys, a technique which has been shown to be unreliable and to seriously underestimate the prevalence of abnormalities (Merrick, 1973), or reported scintigrams without reference to radiographs. Others contain insufficient information for assessment. It has, however, been suggested that, because of the low detection rate and high percentage of false positives, routine scintigraphy is not indicated in asymptomatic subjects.

Our findings do not support this view. We identified skeletal deposits in 53 out of 139 asymptomatic patients (38%), a figure similar to that reported by Kies et al (1978) and by Oyamada et al (1978). The survival of those with occult metastases was significantly shorter than that of those without (Fig. 4) ($\chi^2 = 9\ 82$, 1 d f.; $p < 0.01$). Skeletal scintigraphy thus gives important prognostic information in asymptomatic patients with apparently localised disease, and may be the only staging investigation required by these patients.

There are additional, economic, grounds for performing scintigraphy in all patients for whom thoracotomy is considered (McNeil, 1984). White et al (1982), using an outcome audit to assess the benefit derived from bone scintigraphy, concluded that examinations performed for a specific clinical indication had a recognisable effect (benefit) on decision making in 22 out of 25 patients being assessed for surgery, in three out of 41 patients where it was performed as a staging procedure and in four of 15 asmyptomatic subjects being followed up. An important observation was that a normal result was as likely to be "beneficial", *i.e* to influence decisions about management, as an abnormal one. The prevalence of abnormal findings is, by itself, not an indication of the usefulness of an investigation. Even if only crude financial considerations are considered, very few operations need to be cancelled to offset the cost of scintigraphy: Donato et al (1979) suggest a ratio of 1 . 10.

Alkaline phosphatase levels

Only half of the patients reported by Williams et al (1977) and Kelly et al (1979) with scintigraphic evidence of skeletal involvement had a raised alkaline phosphatase level In the majority it was less than 10% above the upper limit of the reference range, while in the former series the alkaline phosphatase level was also raised in 45 patients without skeletal deposits. This is in accord with the findings of Cowan and Young (1973), who found that only 38 out of 100 patients with skeletal metastases from an unspecified mixture of primary neoplasms had a normal alkaline phosphatase level. Hooper et al (1978), on the other hand, reported that it was raised in all of their patients with a scintigraphic abnormality

In the present series the alkaline phosphatase level was recorded as elevated in 13% of patients with abnormal skeletal scintigraphy However, 47% of subjects with a raised alkaline phosphatase level did not have secondary bone lesions In a few cases, the cause was Paget's disease (Merrick & Merrick, 1985), healing fractures or osteomalacia, in the majority, pathology was extraosseous. Greater tissue specificity may be obtained using assays of isoenzymes, but information about the nature, extent and localisation of disease is still absent. Indeed, as with carcinoma of the prostate (Merrick et al, 1985), this specificity may reduce the sensitivity of the test.

A raised alkaline phosphatase level is, thus, an indication for performing skeletal scintigraphy, because it identifies a group with a high probability of skeletal pathology, but does not indicate the site of disease, whether it is benign or malignant, nor whether solitary or multiple. In many cases the skeleton is not involved. A normal value does not exclude bone metastases Such evidence as is available suggests that alkaline phosphate level is not an important prognostic factor in lung cancer.

Accuracy

No single parameter unambiguously defines the clinical value of a test. The accuracy, true positive rate and true negative rate are all affected by the prevalence of the condition in the population under investigation. In general, the most useful indices are the predictive value of a positive test and that of a negative result (Goris, 1985). Bone scintigraphy combines high sensitivity for the detection of focal skeletal abnormalities with poor specificity in differential diagnosis. With lung, as with other tumours, high false positive rates have been recorded only when scintigraphy was reported in isolation (Ramsdell et al, 1977), or the radiographs and scintigrams were reported separately (Kies et al, 1978). False positives in general indicate the employment of inappropriate criteria for interpretation, or radiological error (Kunkler et al, 1985).

In the present series only those patients with unequivocal confirmation of at least one metastasis were accepted as having had a positive diagnosis. In some cases this was confirmed by a review of existing radiographs, but more commonly, additional planar or tomographic projections of precisely defined regions were obtained after scintigraphy. Using this approach the "scan positive, radiograph negative" patients described in earlier series were found to be uncommon The diagnosis was confirmed in all patients examined post-mortem and by clinical and radiological follow-up in the others. The number of cases considered equivocal is largely a reflection of how vigorously the diagnosis is pursued. Thus, eight out of 57 patients examined post-mortem (14%) were in this category, in three of whom deposits were confirmed. The condition of these patients had deteriorated before adequate radiographs could be obtained.

The false positive rate can be reduced to zero, as in the series by Williams et al (1977) and Donato et al (1979) and the present one, only if an adequate clinical history is available and appropriate radiographic projections of all scintigraphically or clinically suspect areas are examined at the same time as the scintigram. Solitary lesions in particular are commonly due to benign processes (Corcoran et al, 1976; Talarico et al, 1982, Tumeh et al, 1985). A history of minor trauma could be elicited from many of our patients with solitary or contiguous lesions, especially in ribs. By reviewing both the radiographs and the scintigrams together, with the clinical history, the significance of radiographic or scintigraphic abnormalities, which in isolation were likely to be discounted or misinterpreted, could often be evaluated. Tomography was considered necessary when there were one or more lesions unexplained and no unequivocal deposits. It was required in relatively few (less than 10%) of the abnormal cases, in most of which simple tomographic techniques were adequate.

False negative examinations are well documented. Sauerbrunn et al (1972) reported five patients (6%) with false negative scintigrams. Nine false negatives were documented in the series of Williams et al (1977) and Donato et al (1979), six in patients with oat-cell carcinoma and three with poorly differentiated squamous carcinoma, a prevalence of 5.6%. In our post-mortem series there were seven false negative scintigrams (13%) and two false negative post-mortem examinations (3.5%), *i.e.*, unequivocal radiological and scintigraphic evidence of bone metastases in areas which were not examined post-mortem. A scintigraphically equivocal area was not examined post-mortem in one further patient. The prevalence of false negative scintigrams was similar in all the major histological types. On review, four were of adequate technical quality, although in one there was an interval of 1 year between scintigraphy and death and, in another, metastases were not visible macroscopically post-mortem 4 months after scintigraphy, but were confirmed on microscopy. In two other patients the scintigraphic examination was incomplete and did not include the region containing the abnormalities—the cervical spine in one and a rib in the mid-axillary line in another. The photographic record in the remaining false negative was too dark to be of diagnostic value and should not have been accepted. Post-mortem examination 1 year later revealed the deposits. There were, therefore, four false negatives out of 54 technically adequate examinations (7.4%). In contrast, all three technically inadequate studies in the post-mortem series proved to be false negatives. This underlines the importance of maintaining rigorous medical control over the technical quality of all examinations. All of the unsatisfactory studies had been accepted by experienced technicians.

Scintigraphy, thus, achieved a sensitivity of 0.89, a non-specificity (false positives/true negatives) of 0.00 and an accuracy of 0.78. For accuracy to be improved, the number of equivocal examinations would have to be reduced. If technical inadequacies in scintigraphy were eliminated and adequate radiographs of every patient with unexplained scintigraphic abnormalities obtained, an accuracy of 0.93 might be achievable. The predictive value of a positive test, using strict criteria, is 1.00, and the predictive value of a negative test, 0.71. There seems little prospect of significantly reducing the incidence of false negative examinations with existing radiopharmaceuticals. In the present series most were due to tumours which provoked an insufficient osteoblastic response to be visible. Radiopharmaceuticals producing a higher contrast between deposits and normal bone might have detected some of these cases, but are unlikely to have visualised all.

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REFERENCES

Abrams, H. L., Spiro, R. & Goldstein, N., 1959 Metastases in carcinoma; analysis of 1000 autopsied cases. *Cancer*, *3*, 74–85.

American Joint Committee for Cancer Staging and End Result Reporting, 1973 Clinical staging system for carcinoma of the lung. (AJC, Chicago)

Auerbach, O., Garfinkel, L. & Parks, V. R., 1975 Histologic type of lung cancer in relation to smoking habits, year of diagnosis and sites of metastases. *Chest*, *67*, 382–387

Bitran, J. D., Bekerman, C & Pinsky, S., 1981 Sequential scintigraphic staging of small cell carcinoma. *Cancer*, *47*, 1971–1975.

Corcoran, R. J., Thrall, J. H., Kyle, R. W., Kaminski, R. J., Johnson, M. C., 1976 Solitary abnormalities in bone scans of patients with extraosseous malignancies. *Radiology*, *121*, 663–667

Cowan, R. J. & Young, K. A., 1973 Evaluation of serum alkaline phosphatase determination in patients with positive bone scans. *Cancer*, *32*, 887–889

Dimmler, U. & Nachbur, B., 1984 Ist die routinemassige Skelettszintigraphie im praoperativen Staging des Bronchialkarzinoms indiziert? *Helvetica Chirurgica Acta*, *51*, 243–246

Donato, A. T., Ammerman, E. G. & Sullesta, O., 1979 Bone scanning in the evaluation of patients with lung cancer. *Annals of Thoracic Surgery*, *27*, 300–304

Festenstein, F. & Weatherstone, R., 1985. Chemotherapy for small cell carcinoma. *British Medical Journal*, *290*, 1078.

Gilbert, H. A. & Kagan, A. R., 1976. Metastases: incidence, detection and evaluation. In *Fundamental Aspects of Metastases*. Ed. by L. Weiss (Elsevier, Amsterdam), pp. 385–405.

Goris, M. L., 1985 *Sensitivity and Specificity of Common Scintigraphic Procedures* (Year Book Medical Publishers, Chicago).

Gravenstein, S., Peltz, M. A. & Pories, W., 1979 How ominous is an abnormal scan in bronchogenic carcinoma? *Journal of the American Medical Association*, *241*, 2523–2524.

Hansen, H. H. & Muggia, F. M., 1972 Staging of inoperable patients with bronchogenic carcinoma with special reference to bone marrow examination and peritoneoscopy. *Cancer*, *30*, 1348–1352

Hooper, R. G., Beechler, C. R. & Johnson, M C, 1978 Radioisotope scanning in the initial screening of bronchogenic carcinoma. *American Review of Respiratory Diseases, 118,* 279–286

Ihde, D. C., Makuch, R. W, Carney, D N., Bunn, P. A., Cohen, M. H., Matthews, M. J., Minna, J D, 1981 Prognostic implications of stage of disease and sites of metastases in patients with small cell carcinoma of lung treated with intensive combination chemotherapy *American Review of Respiratory Diseases, 123,* 500–507.

Kelly, R. J., Cowan, R J, Ferree, C B, Raben, M. & Maynard, C D, 1979. Efficacy of radionuclide scanning in patients with lung cancer. *Journal of the American Medical Association, 242,* 2855–2857.

Kies, M S, Baker, A. W. & Kennedy, P S, 1978. Radionuclide scans in staging carcinoma of lung *Surgery, Gynecology and Obstetrics, 147,* 175–176.

Komaki, R, Cox, J D & Eisert, D. R., 1977. Irradiation of bronchial carcinoma—II Pattern of spread and potential for prophylactic irradiation. *International Journal of Radiation Oncology, Biology, Physics, 2,* 441–446

Kunkler, I. H., Merrick, M V & Rodger, A., 1985. Bone scintigraphy in breast cancer—a 9-year follow-up. *Clinical Radiology, 36,* 279–282

Levenson, R M, Sauerbrunn, B. J. L., Ihde, D C, Bunn, P. A., Cohen, M. H & Minna, J D, 1981. Small cell lung cancer: radionuclide bone scans for assessment of tumor extent and response *American Journal of Roentgenology, 137,* 31–35.

Little, A G., DeMeester, T R. & MacMahon, H, 1983. The staging of lung cancer. *Seminars in Oncology, 10,* 56–70

Matthews, M J, 1976. Problems in morphology and behavior of bronchopulmonary malignant disease In *Lung Cancer, Natural History, Prognosis and Therapy.* Ed. by L. Israel & A. P. Chahinian (Academic Press, New York), pp 23–62

Matthews, M J. & Gazdar, A F, 1981. Pathology of small cell carcinoma of the lung and its subtypes A clinico-pathologic correlation. In *Lung Cancer 1.* Ed. by R. B Livingston (Martinus Nijhoff, The Hague), pp 283–306

Matthews, M J, Kanhouwa, S & Pickren, J, 1973 Frequency of residual and metastatic tumour in patients undergoing curative surgical resection for lung cancer. *Cancer Chemotherapy Reports, 4, Suppl 4,* 63–67.

Maurer, L H. & Pajak, T. F, 1981 Prognostic factors in small cell carcinoma of lung. a cancer and leukaemia group B study. *Cancer Treatment Reports, 65,* 767–774.

McNeil, B J., 1984 Value of bone scanning in neoplastic disease. *Seminars in Nuclear Medicine, 14,* 277–286

McNeil, B J, Collins, J. J & Adelstein, S. J., 1977 Rationale for seeking occult metastases in patients with bronchial cancer. *Surgery, Gynecology and Obstetrics, 144,* 389–393.

Merrick, M V, 1973. Detection of skeletal metastases: a comparison of three radioisotope techniques using ^{18}F and radiology *British Journal of Radiology, 46,* 968–971

——1984. *Essentials of Nuclear Medicine.* (Churchill Livingstone, Edinburgh), pp. 145–152

——1986. Isotope techniques in oncology. In *Investigative Techniques in Oncology.* Ed by N M. Bleehen (Springer Verlag, Stuttgart), in press.

Merrick, M V, Ding, C. L & Chisholm, G. D., 1985. The prognostic significance of alkaline phosphatase and bone scintigraphy in carcinoma of prostate. *British Journal of Urology, 57,* 715–720

Merrick, M V & Merrick, J. M., 1985. Observations on the natural history of Paget's disease *Clinical Radiology, 36,* 169–174

Morstyn, G, Ihde, D. C., Lichter, A. S., Bunn, P A., Carney, D. N, Glatstein, E. & Minna, J. D, 1984 Small cell lung cancer 1973–1983: early progress and recent obstacles. *International Journal of Radiation Oncology, Biology, Physics, 10,* 515–539.

Napoli, L. D., Hansen, H H, Muggia, F M. & Twigg, H. L, 1973. The incidence of osseous involvement in lung cancer with special reference to the development of osteoblastic changes. *Radiology, 108,* 17–21.

Ohnoshi, T, Hiraki, S., Nakata, Y, Miyake, K., Harada, J. Ozawa, S, Tamura, T., Seto, T., Miyai, M., Tanaka, T & Kimura, I, 1982 Bone marrow examination for detection of metastases in patients with bronchogenic carcinoma an evaluation of 107 patients. *Acta Medica Okayama, 36,* 141–146

Oyamada, H, Tabei, T, Yoneyama, T., Eguchi, K., Orii, H, Terui, S, 1978 Whole body bone scintigram and stage classification of the patients with adenocarcinoma of lung *Tohoku Journal of Experimental Medicine, 124,* 145–151.

Ramsdell, J. W., Peters, R. M., Taylor, A. J., Alazraki, N. P & Tisi, G. M, 1977 Multiorgan scans for staging lung cancer. Correlation with clinical evaluation. *Journal of Thoracic and Cardiovascular Surgery, 73,* 653–659.

Roswit, B., Patno, M. E. & Rapp, R, 1968 The survival of patients with inoperable lung cancer. A large scale randomised study of radiation therapy versus placebo *Radiology, 90,* 688–697.

Sauerbrunn, B. J L, Hansen, H H & Napoli, L. D., 1972 Strontium bone scans in carcinoma of the lung, a comparative prospective study. *Journal of Nuclear Medicine, 13,* 465–466

Scott, J S & Adams, F. G, 1974 The place of scintiscanning using ^{87m}Sr in the detection of osseous metastases. *Clinical Radiology, 25,* 497–505

Scottish Cancer Registry, 1984 *Cancer Registration Statistics 1971–1980* (Scottish Health Service Common Services Agency, Edinburgh)

Shirazi, P. H, Rayudu, G V S & Fordham, E. W., 1974 ^{18}F bone scanning a review of indications and results in 1500 scans *Radiology, 112,* 361–368.

Spiro, S. G., 1985. Chemotherapy for small cell lung cancer *British Medical Journal, 290,* 413–414

Talarico, L J, Abdel-Dayem, H. M & Leslie, E V, 1982 Significance of rib lesions in pyrophosphate bone scans *Journal of Nuclear Medicine, 23,* 29

Tofe, A J, Francis, M. J. & Harvey, W J., 1975. Correlation of neoplasms with incidence and localisation of skeletal metastases an analysis of 1355 diphosphonate bone scans. *Journal of Nuclear Medicine, 16,* 986–989

Tumeh, S S., Beadle, G. & Kaplan, W D, 1985 Clinical significance of solitary rib lesions in patients with extraskeletal malignancy *Journal of Nuclear Medicine, 26,* 1140–1143

Turner, P. & Haggith, J W, 1981 Preoperative radionuclide scanning in bronchogenic carcinoma. *British Journal of Diseases of the Chest, 75,* 291–294.

White, D M, McMahon, L. J. & Denny, W F., 1982 Usefulness outcome in evaluating the utility of nuclear scans of the bone, brain and liver in bronchogenic carcinoma patients *American Journal of Medical Sciences, 283,* 114–118.

Williams, S. J., Green, M & Kerr, I H, 1977 Detection of bone metastases in carcinoma of bronchus. *British Medical Journal, 274,* 1004.

1986, *The British Journal of Radiology*, 59, 1195–1201 DECEMBER 1986

Regional hyperthermia for extensive pelvic tumours using an annular phased array applicator: a feasibility study

By G. C. W. Howard, B.Sc., M.R.C.P., F.R.C.R., *V. Sathiaseelan, Ph.D., †G. A. King, M.D., ‡A. K. Dixon, M.A., M.R.C.P., F.R.C.R., A. Anderson, B.Sc., S.R.N., N. M. Bleehen, F.R.C.P., F.R.C.R., F.A.C.R. (Hon.)

University Department and Medical Research Council Unit of Clinical Oncology & Radiotherapeutics, and ‡University Department of Radiology, Clinical School, Hills Road, Cambridge CB2 2QH

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ABSTRACT

Twenty patients with extensive pelvic tumours have been treated with radiotherapy and regional hyperthermia using an annular phased array applicator (APA). The majority of patients had bulky disease with a mean tumour volume of 206 cm^3. In 63 of 67 attempted treatments heating was achieved, temperatures in excess of 42°C being reached in the pelvis in 78%. Heat doses, however, were low, only 41% of treatments exceeding 5 min equivalent at 43°C. Treatment was usually limited by acute toxicity and, although this was marked, it was of short duration and no long-term sequelae have been noted. With gain in operator experience, later treatments have achieved improved thermal doses. Response was difficult to assess but we have documented responses in six of 12 assessable patients. Palliation has been achieved in all patients with symptoms. Preliminary attempts to shift the region of maximum heating by phase variations in the APA output are promising, and this technique should improve the quality of treatments and reduce toxicity. The APA is thus capable of inducing pelvic regional hyperthermia, and a randomised controlled study is now planned to assess the value of pelvic hyperthermia as a treatment modality.

Hyperthermia, both alone and in combination with other treatment modalities, has now been extensively investigated in both the laboratory and the clinic. Controlled clinical studies on superficial tumours now confirm a synergistic interaction between radiotherapy and hyperthermia with an increase in both complete and partial response rates (Arcangeli et al, 1983; Overgaard, 1984) and possibly an increase in speed and duration of response (Scott et al, 1984). In addition, the possibility of achieving a therapeutic gain by suitable timing of the two modalities has also been demonstrated (Arcangeli et al, 1983). The interaction between radiotherapy and hyperthermia has not been demonstrated in deep-seated tumours as, until recently, techniques for heating at depth were not available. Most experience of regional hyperthermia has been in the use of hyperthermic limb perfusion, often in combination with chemotherapy (Stehlin et al, 1979).

A number of techniques are now being investigated for inducing regional hyperthermia using capacitive, inductive and radiative methods of electromagnetic heating. The latter method has been used in the commercially available annular phased array (APA) produced by the BSD corporation, Salt Lake City. Experience with this machine is limited, the only large series reported being that of Sapozink et al (1984) using the prototype. Following the commission of an APA in our department, a feasibility study was initiated to assess the capability of the equipment to heat at depth in patients with pelvic tumours.

METHODS

The annular phased array

The APA is an applicator comprising 16 radio-frequency (RF) radiators arranged in two circles of eight. The dimensions of the octagonal aperture are such that constructive interference occurs at its centre, leading to preferential energy deposition and, thus, heating in this region. The patient is positioned within the aperture and coupled to the applicators by three bolus bags filled with deionised water (Fig. 1). The external electric field strength is measured by four electric field ("E" field) probes positioned on the patient's skin. The APA is powered by a 2 kW amplifier which can be operated in the frequency range 50–100 MHz.

Thermometry

Temperatures were measured with non-perturbing high-resistance thermistors (Bowman probes) calibrated

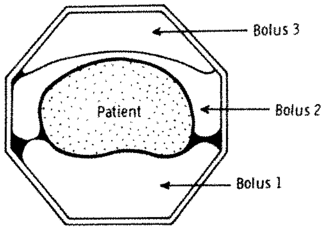

FIG. 1.
Diagrammatic cross-section of the annular phased array.

Present address: *Physics Section, Division of Radiation Oncology, Mallinckrodt Institute of Radiology, St Louis, USA; †Department of Radiology, SUNY Upstate Medical Center, Syracuse, New York, USA.

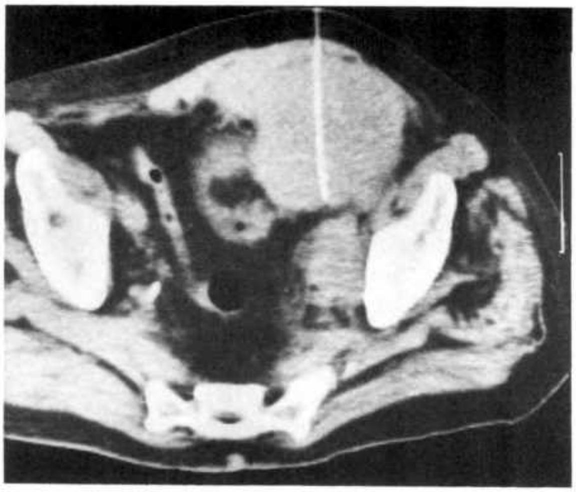

FIG. 2. *Case 11.*
A CT section across the pelvis showing bladder tumour with catheter in place.

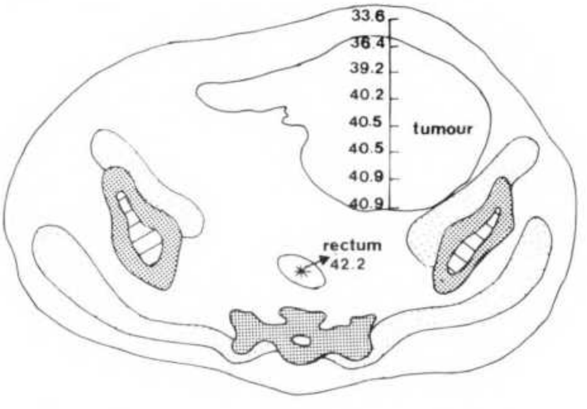

FIG. 3.
Temperature profile across the tumour shown in Fig. 2 during a treatment. Core temperature 39.1°C.

against two National Bureau of Standards traceable thermistor probes. Four probes were available for use in regional hyperthermia treatments. They were inserted into normal and tumour tissues along 16-gauge blind-ended Teflon catheters (Deseret Medical Inc., USA). Usual pelvic sites for temperature measurement were the rectum, vagina and urinary bladder, an oral probe being used to monitor changes in core temperature. These intracavitary probes were useful for measuring normal tissue temperatures and, often, were situated adjacent to tumour tissue. Intratumour catheters were also inserted wherever possible. In patients where the tumour was palpable, this could be performed direct, percutaneously, per vagina or per rectum. With more deeply situated tumours, catheters were inserted under the control of computed tomography (CT) (Fig. 2). When possible, probes were tracked during treatment along the catheter to measure the temperature profile across the tumour (Fig. 3).

Patient selection

Patients were selected if they had extensive pelvic tumours considered to be unlikely to respond well to standard treatment modalities. Treatments were limited to the pelvis as this has been shown to be the site most easily heated with the APA (Sapozink et al, 1984), and heating of more proximal regions often results in unacceptable systemic hyperthermia. In addition, the normal body orifices allow access to deep pelvic tissues for thermometry. Thus, the majority of patients had extensive pelvic recurrences of rectal, cervical and bladder tumours. Many patients had been heavily pre-treated with radiation and/or chemotherapy; however, a few previously untreated patients with particularly extensive tumours were also considered suitable.

Patients need to be relatively fit to tolerate the possible stress of regional hyperthermia and a performance status of 2 or less (World Health Organization (WHO), 1979) is desirable. In particular, patients with known ischaemic heart disease were excluded in view of the transient changes in pulse rate and blood pressure seen during treatment. Patients also needed to be emotionally stable and well motivated. All patients gave full informed consent after the experimental nature of the treatment had been explained to them.

For patients considered suitable for treatment, further investigations included estimations of haemoglobin, white cell count, and platelets, serum urea and electrolytes, liver function tests and protein electrophoresis. Serum creatine kinase and lactate dehydrogenase estimations, together with the prothrombin time, thrombin time and kaolin partial thromboplastin time were also measured. Cardiac enzyme estimations and a coagulation screen were carried out because of the known cardiovascular stress induced by these treatments and the coagulopathies reported following whole-body hyperthermia (Engelhardt, 1984). Pelvic CT was performed to document tumour size and suitability for CT-guided catheter placement. Where the tumour approximated to a sphere or ellipsoid, its volume was calculated using the formula $4\pi abc/3$; where a was half the length; and b and c were the maximum radii at 90° to each other.

Radiotherapy

All hyperthermia treatments were combined with radiotherapy. The latter was planned to suit the individual patient's requirements regarding dose and technique. In all cases, planned volumes were treated to encompass known disease. When there had been previous radiotherapy, the most usual regimen was 20 Gy in 10 daily fractions over 12 days, and in these cases hyperthermia was given twice weekly on a

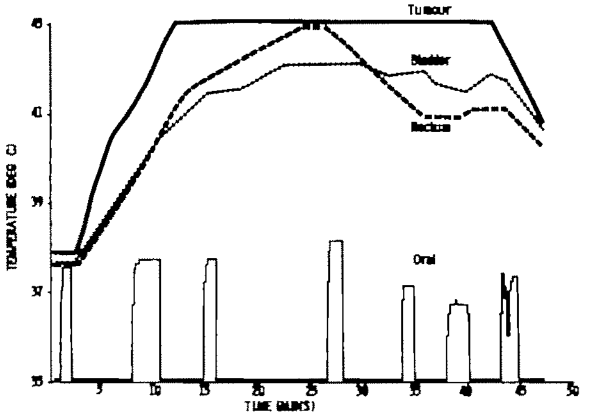

FIG. 4 *Case 9*
Temperature profile of a treatment.

Monday–Thursday, Tuesday–Friday basis. Where there had been no prior radiotherapy, higher doses were given, usually 50 Gy in 25 daily fractions over 35 days in view of the large treated volume in the majority of patients. In these cases hyperthermia was given once a week, as our early experience indicated that patients would rarely accept more than a total of five hyperthermia treatments. On all occasions the hyperthermia treatment was given within 1 h after irradiation.

Hyperthermia treatment procedure

Pre-treatment preparation involved ensuring an empty rectum before heating to avoid local hot spots in faecal masses, and occasionally a sedative for particularly anxious patients (diazepam 10 mg orally). A urinary catheter was inserted to drain residual urine which may result in localised heating; this also provided access to the bladder for thermometry. Other thermistors were placed in the rectum and vagina as indicated and into a catheter inserted into the tumour when this was available. The patient was then transferred onto a stretcher passing through the aperture of the APA. The latter was then guided over the patient until the pelvis was positioned at its centre. Saline bags were placed between the legs and behind the neck of the patient to avoid local hot spots in these regions where the body contour narrows, leading to convergence of the "E" fields (Turner, 1984).

Power was then applied through the APA until a temperature rise of about 0.3°C/min was obtained, which usually required between 1.0 kW and 1.6 kW. This was continued until the desired temperature of 43°C was reached or toxicity necessitated power reduction. During treatment, blood pressure and pulse were monitored automatically and the oral temperature was measured intermittently. When necessary, the room temperature was reduced in order to maintain the core temperature at acceptable levels; also, cooled water could be circulated through the bolus bags and a fan directed onto the patient's face and torso. Our planned treatment was to maintain the tumour at 43°C for 30 min while keeping normal tissue temperature below this. An example of such a treatment is illustrated in Fig. 4.

Following the treatment, quarter-hourly measurements of temperature, pulse and blood pressure were recorded for a further period of 1 h. In all cases these had returned to normal at the end of this time. The overall time for treatment, including catheter insertion, sometimes took up to 2 h. In this pilot study, patients undergoing regional hyperthermia were admitted for at least one night for further observation, although this may prove to be unnecessary as a routine.

RESULTS

Hyperthermia

Sixty-seven treatments were performed in the APA on 20 patients, an average of 3.4 treatments per patient. Details are given in Table I. All patients had histologically proven pelvic tumours, some extending into the lower abdomen. The majority of patients had extremely bulky disease as estimated by CT, with volumes ranging from 10 cm^3 to 679 cm^3 (mean 206 cm^3). Eight patients had colorectal tumours, five had carcinoma of the cervix, three had carcinoma of the bladder, one each had carcinoma of the prostate, uterus and vagina and one had pelvic sarcoma. Patients' ages varied from 32 years to 71 years with a mean of 59 years. Twelve patients had previously been treated with radiotherapy, doses ranging from 24 Gy to 60 Gy, and 12 patients had undergone surgery previously. Of the 67 treatments attempted, 63 are assessable. On the remaining four occasions, heating was never achieved due to equipment failure. During our initial experience technical problems were a significant factor, limiting temperatures achieved in a further 10 treatments. The most persistant problem was a frequency-dependent interference between the APA and the thermometry system. This may be eliminated by changing the frequency by 5–10 MHz when it occurs. In general, technical difficulties seem to have been mainly teething problems, at least in part due to our own inexperience in the use of this equipment, and have now become rare.

There are two ways of assessing the success of these treatments, the first being to find out on how many occasions certain specified temperatures were reached. This approach assesses the technical ability of the machine to heat at depth. The second is by the calculation of a "heat dose" which takes into account the time–temperature relationship. Overall, in our series 43°C was reached at depth within the pelvis in 29 (46%) of treatments and 42°C in a further 20 (32%) (Fig. 5). Thus, if 42°C is considered to be a therapeutically useful temperature, this was reached in 78% of treatments. "Heat doses" were calculated as minutes

TABLE I

PATIENT AND TREATMENT DATA

Case	Age (years)	Site of primary tumour	Tumour volume (cm³)	Radiation			No. of hyperthermia treatments	Response		
				Dose (Gy)	Number of fractions	Time (days)		Objective	Palliation	Survival (months)
1	66	Rectum	NA	14	7	9	2	SD	—	9
2	59	Uterus	210	50	22	45	3	PR	Yes	12+
3	69	Rectum	10	12	4	14	3	SD	Yes	12+
4	46	Cervix	216	50	23	35	2	NA	—	1
5	66	Colon	53	18	6	11	3	NA	Yes	2
6	66	Bladder	NA	20	9	39	7	SD	—	8+
7	43	Colon	28	50	25	35	4	PR	Yes	8+
8	40	Cervix	NA	20	10	12	3	SD	—	6+
9	36	Cervix	84	20	10	14	4	SD	Yes	6+
10	68	Cervix	29	20	10	15	1	NA	NA	4
11	66	Bladder	317	20	10	12	4	SD	Yes	5
12	68	Pelvic sarcoma	647	20	10	12	3	PR	Yes	4+
13	55	Rectum	679	40	20	28	2	CR	Yes	2
14	63	Rectum	246	50	25	35	5	PR	Yes	3+
15	32	Cervix	142	65	33	49	2	PR	Yes	2+
16	68	Prostate	126	30	15	23	4	—	Yes	2+
17	71	Vagina	561	20	10	12	3	—	Yes	1+
18	64	Bladder	96	30	15	19	4	—	—	1+
19	69	Rectum	12	36	12	32	4	—	Yes	1+
20	63	Rectum	53	22	11	15	4	—	—	1+

NA = not assessable, SD = static disease, PR = partial response, CR = complete response.

equivalent at 43°C (min/eq/43°C), using a standard formula (Dunlop et al, 1984). This approach to assessment was less encouraging, with the desired dose of 30 min/eq/43°C achieved only once. Doses between 15–29.9 and 5–14.9 min/eq/43°C were achieved in seven and 18 treatments, respectively, with doses less than this on 37 occasions (Fig. 6). Thus, in 41% of treatments heat doses in excess of 5 min/eq/43°C were achieved.

Some studies have indicated a tendency for intratumour temperatures to be higher than normal tissues (Storm et al, 1979). In this series intratumour probes were present in 11 of the 20 patients, and intratumour temperatures exceeded those of normal tissues in 50% of treatments. However, overall heat doses achieved were comparable with those elsewhere in the pelvis The significance of this is doubtful as there are marked temperature variations across the heated volume, as illustrated in Fig. 3 where a differential of 4.5°C existed across the tumour.

With increasing experience in the use of the machine and more careful patient selection, the number of treatments per patient and the temperatures achieved have increased, but there is a discrepancy between the high proportion of treatments reaching therapeutic temperatures and the low heat doses recorded. This is because high intrapelvic temperatures are poorly tolerated for extended periods of time.

Toxicity

In all but two treatments the duration of heating and the temperatures achieved were limited by the acute toxicity of the treatment (Table II). There were 74 instances of some form of toxicity limiting treatment. During some treatments patients complained of more than one side-effect, necessitating power reduction or treatment termination. In 28 cases the treatment-limiting toxicity was the general discomfort of the patient; this was a combination of the uncomfortable treatment position and the effects of the induced systemic heating. The second most common problem, occurring in 15 treatments, was localised discomfort within the pelvis, relieved by a reduction in RF power and probably temperature-related. This sensation was often difficult for the patient to define but was not usually described as a feeling of heat or burning. Other side-effects were less common, but of note is that an unacceptable tachycardia or rise in core temperature limited only five and nine treatments, respectively. Other recorded treatment-limiting factors were anxiety, normal tissue temperatures exceeding 43°C and pain not related to heating, such as arthritic joint pain precipitated by the treatment position. It is of note that lack of RF power never limited the treatments. Other acute side-effects which were not severe enough to limit treatment are shown in Table III. Tingling of either the arms or legs has been noted on four occasions but these

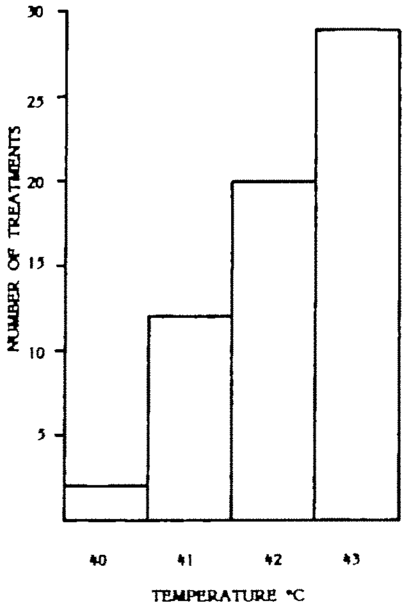

Fig. 5.
Maximum temperatures reached in 63 treatments

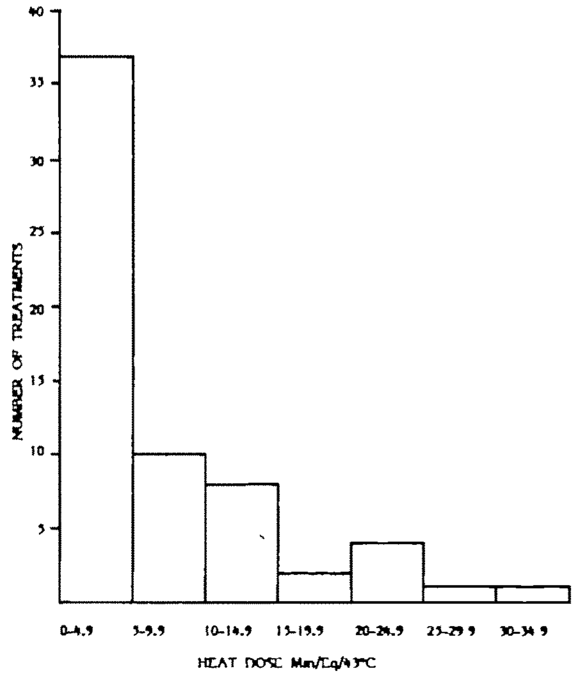

Fig. 6.
Maximum heat dose achieved in 63 treatments

did not persist and there has been no resultant neurological loss. Drowsiness was noted on four occasions, usually associated with an oral temperature in excess of 39.5°C. On two occasions small burns occurred on the wrist following the patient touching the side of the APA with his watch. All jewellery is now removed before treatment.

Although acute toxicity was marked, it was invariably of short duration and usually subsided within 1 h of treatment. More prolonged symptoms have occasionally been noted. A generalised tiredness, usually lasting only 24–48 h, sometimes developed after treatment but some patients complained of general malaise and tiredness for a more prolonged period. This may be related as much to the radiotherapy as to the hyperthermia. In four patients frequency of micturition with dysuria, sometimes accompanied by a documented urinary tract infection, was noted as a result of the repeated urinary catheterisations.

TABLE II

Acute treatment-limiting toxicity: number of events seen during 63 treatments of 20 patients

Toxicity	No. of times recorded
Generalised patient discomfort	28
Pelvic discomfort	15
Rise in core temperature (oral temperature >39.5°C)	9
Tachycardia pulse >150	5
Anxiety	4
Pain not related to heating	4
Hypertension: diastolic pressure > 105 mm Hg	4
Hypotension: systolic pressure < 100 mm Hg	1
Normal tissue temperature >43°C	2
None	2

In two patients, both of whom had an abnormal pre-treatment ECG, cardiographic changes were noted after treatment. In one there was "T" wave inversion in the anterior chest leads and in the second patient a bigeminal rhythm developed. In both cases the ECG reverted to the pre-treatment appearance within 24 h. In neither case was there an associated rise in cardiac enzymes. Transient elevation of the serum non-cardiac creatine kinase isoenzyme was noted in three patients following our initial hyperthermia treatments.

TABLE III

Other acute toxicity

Toxicity	No. of times recorded
Joint pain	9
Peripheral paraesthesiae	4
Drowsiness	4
Faintness	2
Burns	2

Subsequently, this enzyme was closely monitored following 30 treatments. In six instances a significant rise occurred, but this did not appear to relate to either intrapelvic or core temperatures recorded during treatment. We noted no effect on the other blood and serum parameters measured; in particular, there was no change in the coagulation studies or cardiac enzymes after treatment

Response

The assessment of response in these patients is difficult, not least because most patients were heavily pre-treated. Furthermore, patients received varying doses of radiation and a variable number and quality of hyperthermia treatments. Of the 20 patients, five have only recently finished treatment, leaving 15 assessable with a minimum follow-up of 2 months. Nine of these patients are alive between 2 months and 1 year after treatment. Six patients have died, four due to tumour progression. There has been one unexpected death in a patient with Stage III carcinoma of the cervix 4 weeks following treatment. The cause of death, although not clear, appeared to be renal failure due to ureteric obstruction by tumour and there would appear to be no reason to implicate the hyperthermia treatment.

There has been a documented response of disease in six patients. In four patients a greater than 50% reduction in tumour volume has been demonstrated by CT, with one further partial response on clinical examination. Complete disappearance of palpable disease occurred in one patient, although this was not documented by CT. In a further six patients disease has remained static for periods from 2 months to 1 year and in three patients disease could not be assessed.

In view of the advanced nature of the disease in all patients, the main goal was symptom control. It is noteworthy in this context that in all patients a degree of palliation, such as reduction in haematuria and improved pain control, was achieved. Late toxicity is as difficult to assess as tumour response but does not appear to be any more marked, or different in nature from that which might be seen in any group of heavily irradiated patients.

Alteration of power distribution

The APA is designed to deposit energy maximally at the centre of the aperture, so that tumours positioned eccentrically within the pelvis may be difficult to heat. The ability to steer the region of maximum energy deposition would, therefore, be of great value Two methods of doing this are being investigated. Phantom experiments indicate that the maximum field strength is moved from posterior to anterior as the frequency is increased from 50 MHz to 70 MHz, with heating at the centre maximal at 60 MHz. Early clinical experience seems to confirm this.

The effect of changes in phase and attenuation to separate quadrants of the APA have been modelled using CT data. This modelling technique has demonstrated how a change in phase to one quadrant will shift the maximum field strength away from the centre of the applicator. During treatments, phase changes may be effected by the addition of a variable length of coaxial cable supplying a quadrant, resulting in a shift of the maximum field strength toward that quadrant (Sathiaseelan et al, 1985).

Figure 7 illustrates a clinical treatment where this technique was used in a patient with a pre-sacral recurrence of a rectal carcinoma. At the beginning of treatment the bladder temperature rose more quickly than that of the tumour. After 10 min the power was switched off, phasing cables inserted to shift the maximum field strength posteriorly and the treatment restarted. It can be seen that preferential heating of the tumour was then achieved, resulting in a more satisfactory treatment.

DISCUSSION

The data presented confirm other studies demonstrating that the APA is capable of heating at depth within the pelvis. In this series of 67 treatments, temperatures in excess of 42°C were reached in 78% of treatments, but were difficult to maintain for a prolonged period due to the acute toxicity of the treatment.

This toxicity, although marked and limiting treatment in the majority of cases, was usually of short duration. There has been no serious late toxicity. Assessment of response is difficult and was not the primary aim of this study. However, it is encouraging that there was palliation of symptoms in the majority of patients.

It would be a great advantage to be able to steer the region of maximum heating toward the tumour-bearing area. Our initial studies on phase adjustment to achieve this are promising. If such steering proves reliable, treatments may be improved and toxicity reduced.

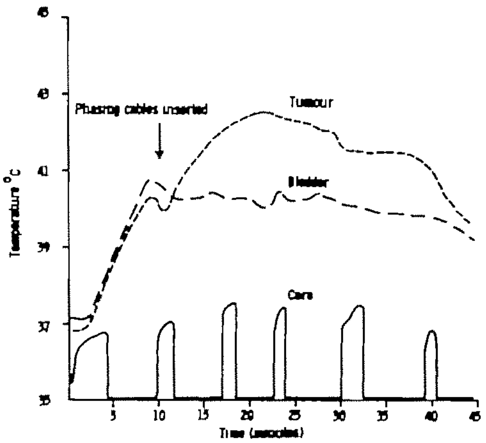

FIG 7. *Case 20.*
Treatment temperature profile demonstrating the use of phasing cables during treatment.

Pelvic regional hyperthermia is a time-consuming and labour-intensive procedure but is a feasible treatment modality. The synergism between radiation and hyperthermia demonstrated for superficial lesions now needs to be confirmed for regional hyperthermia in randomised controlled trials.

REFERENCES

Arcangeli, G., Cividalli, A., Lovisolo, G. & Nervi, C., 1983. Clinical results after different protocols of combined local heat and radiation. *Strahlentherapie, 159*, 82–89.

Dunlop, P., Dickinson, R., Hand, J. & Field, S., 1984. The use of thermal dose in the clinical application of localised hyperthermia. In *Proceedings of the 4th International Symposium on Hyperthermic Oncology*. Ed. by J. Overgaard, (Taylor & Francis, London), Vol 1, pp. 187–190.

Engelhardt, R., 1984. Whole body hyperthermia Methods and clinical results. In *Proceedings of the 4th International Symposium on Hyperthermic Oncology*. Ed. by J. Overgaard, (Taylor & Francis, London), Vol. 2, pp. 263–276.

Overgaard, J., 1984. Rationale and problems in the design of clinical studies. In *Proceedings of the 4th International Symposium on Hyperthermic Oncology*. Ed. by J. Overgaard, (Taylor & Francis, London), Vol. 2, pp. 325–338.

Sapozink, M., Gibbs, F., Gates, K. & Stewart, R., 1984 Regional hyperthermia in the treatment of clinically advanced, deep seated malignancy. Results of a pilot study employing an annular array applicator. *International Journal of Radiation Oncology, Biology, Physics, 10*, 775–786.

Scott, R., Johnson, R., Story, K. & Clay, L., 1984. Local hyperthermia in combination with definitive radiotherapy: increased tumour clearance, reduced recurrence rate in extended follow up *International Journal of Radiation Oncology, Biology, Physics, 10*, 2119–2123

Sathiaseelan, V., Iskander, M., Howard, G. C. W., Crocker, S. & Bleehen, N. M., 1985 Theoretically predicted effect of phase and amplitude variation on the electromagnetic power deposition patterns for the annular phased array hyperthermia system *Strahlentherapie, 161*, 549.

Stehlin, J. S., Giovanella, B., de Ipolyi, P. D. & Anderson, R. F., 1979. Results of eleven years' experience with heated perfusion for melanoma of the extremities. *Cancer Research, 39*, 2255–2257.

Storm, F. K., Harrison, W. H., Elliott, R. S. & Morton, D. L., 1979. Normal tissue and solid tumour effects of hyperthermia in animal models and clinical trials. *Cancer Research, 39*, 2245–2251

Turner, P. F. 1984. Regional hyperthermia with an annular phased array IEEE Transactions in Biomed Eng. Vol BME 31 No 1: 106–114.

WHO, 1979. *Handbook for Reporting Clinical Results of Cancer Treatment*. WHO Offset Publications, No. 48, 7

Book review

Diagnosis and Treatment of Carcinoma of the Cervix in Developing Countries. Ed. by R. F. Mould and K. Tungsubutra, pp. xix+349+index, 1985 (Adam Hilger Ltd, Bristol), £35.00.
ISBN 0-85274-561-3

This book is a report on the most recent meeting of the International Working Party held in Thailand in 1985. The Working Party, which meets in developing countries every 2 years, consists of a group of radiotherapists, gynaecologists, medical physicists and others with a specific interest in common, that is the treatment of carcinoma of the cervix in developing countries The magnitude of this problem is borne out by several of the papers given at this meeting, as carcinoma of the cervix is the commonest cancer in women in Asia, Africa and Latin America. For instance, out of every four patients with cancer in India, one will have cervical carcinoma The problem is not only one of numbers, there is also a lack of trained personnel, equipment and resources In addition, patients frequently are desperately poor and usually reside in rural areas with virtually no transport and, because of their ignorance of cancer, seek help only when they have advanced disease

In order to improve this dismal picture, the International Atomic Energy Agency with the help of the World Health Organization and the Italian government have, on the basis of the work of the Working Party, set up a pilot project in Egypt to establish brachytherapy as a first step of a radiotherapy service for countries in Asia and Africa that have no radiotherapy treatment centres at the present time. As the various papers point out, there are many problems, as the system used must be safe, simple enough to be carried out by, for instance, gynaecologists with no radiotherapy experience, and incorporate practical dosimetry to compensate for the absence of medical physicists. The Working Party has worked out techniques for the pilot project using the Amersham manual afterloading system. Other contributors detail experience with remote afterloading, which is ideal for use in those countries where a large number of patients need to be treated by a minimum number of staff on an out-patient basis The work presented by these experts will be found helpful by all users of afterloading machines in regard to equipment, dosage, fractionation and the prevention of complications.

In conclusion, I would recommend this book to radiotherapists interested in carcinoma of the cervix as a world-wide problem and to users of remote intracavitary afterloading machines who will find in it much useful information

H. E LAMBERT

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Total lymphoid irradiation of intractable rheumatoid arthritis

By M Herbst, H. Fritz and R. Sauer

Department of Radio-oncology, University of Erlangen-Nuremberg, West Germany

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ABSTRACT

Eleven patients with intractable rheumatoid arthritis were treated with fractionated total lymphoid irradiation at a total dose of 20 Gy. Lasting improvement in clinical symptoms was found in four patients during treatment and the remaining patients experienced a similar benefit within 2 months of irradiation. There was marked reduction in exacerbations and the number of joints involved. Morning stiffness, joint swelling and tenderness decreased. Complications included severe fatigue during treatment and acute bacterial arthritis in multiple joints in one patient. Four of the patients have since died, one of renal failure and another of cardiogenic shock following surgery 3 and 24 months after total lymphoid irradiation. Both had generalised amyloidosis. The third patient developed joint empyema and died of toxic cardiac failure. The fourth died 3 months after resection of a Kaposi's sarcoma complicated by wound infection which responded to treatment. Immunologically, total lymphoid irradiation resulted in suppression of the absolute lymphocyte count and a reduction in T-helper cells, while the number of T-suppressor cells remained unchanged. These data provide evidence of T-cell involvement in the pathogenesis of rheumatoid arthritis. Total lymphoid irradiation can induce sustained improvement in clinical disease activity, but severe, possibly fatal, side-effects cannot be ignored.

Total lymphoid irradiation is an effective and reliable treatment modality for patients with Hodgkin's disease (Kaplan, 1980b). It leads to a lasting depression of various immunological parameters (Bobrove et al, 1975; Fuks et al, 1976; Kaplan, 1980a; Twomey & Rice, 1980). Without chemotherapy it does not increase the risk of bacterial infection or secondary haematological malignancies (Fuks et al, 1976; Kaplan, 1980b). Bobrove et al (1975) and Fuks et al (1976) demonstrated a reduction in cell-bound immunity after total lymphoid irradiation. A reduction in the T lymphocytes and their subpopulations persisting for more than 10 years was observed in peripheral blood. The same groups investigated the immunosuppressive effect of total lymphoid irradiation in animals. In mice subjected to total lymphoid irradiation (17 fractions of 2.0 Gy each), rejection of skin grafts was greatly delayed (Slavin et al, 1976), and no graft-versus-host reactions developed following bone marrow transplantation (Gottlieb et al, 1980).

The immunosuppressive effect of total lymphoid irradiation having been established, further studies were done to determine its effect in autoimmune diseases. In mice with a lupus erythematoses-like disease subjected to total lymphoid irradiation, Kotzin & Strober (1979) observed a regression of glomerulonephritis and a prolongation of survival vis-à-vis controls. These results showing an immunosuppressive effect of total lymphoid irradiation were supported by experiments done by Schurmann et al (1981) on rats with arthritis induced by Freund's adjuvant. The therapeutic results of total lymphoid irradiation were appreciably better than those obtained with irradiation of the joints alone. Combined joint and total lymphoid irradiation yielded the best results with respect to remission and late functional capability of these joints.

The non-steroidal treatment of rheumatoid arthritis with anti-inflammatory agents, chloroquine derivatives, gold salts, and D-penicillamine is not always satisfactory. Immunosuppressive drugs and cytotoxic agents, such as cyclophosphamide, control the disease only in individual cases.

Since it is well tolerated and has few side-effects, total lymphoid irradiation is considered by Strober et al (1981) and Trentham et al (1981) to be an alternative to cytotoxic therapy. In their first pilot study, Strober et al (1981) treated the infradiaphragmatic lymph nodes, including the spleen, in patients with intractable rheumatoid arthritis, with a total dose of up to 40 Gy. In four out of six patients, they observed a distinct improvement in joint symptoms (swelling, morning stiffness, mobility) and no serious side-effects (fatigue or nausea).

In further studies, Strober et al (1983) examined the effect of a total lymphoid irradiation dose up to 20 Gy (considerably less than the dose used to treat Hodgkin's disease) in 11 patients. Trentham et al (1981) studied the effect of total lymphoid irradiation with a dose of up to 30 Gy in 12 patients (Strober et al, 1981; Trentham et al, 1981; Strober et al, 1983; Brahn et al, 1984). Strober et al considered a total dose of 20 Gy to be sufficient, after Gottlieb et al (1980) demonstrated better tolerance to alloantigens and had seen a prolongation of survival time in dogs and monkeys following total lymphoid irradiation. Subsequently, the clinical results confirmed that total lymphoid irradiation with a 20 Gy dose is sufficient for immunosuppres-

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Address for reprints Manfred Herbst, M D., Associate Professor of Medicine, University Erlangen-Nuremberg, Universitatsstrasse 27, 8520 Erlangen, West Germany

sion. Whether a smaller dose produces the same effect has not yet been investigated clinically.

METHODS

In 1982 the Radio-oncology Department of the University of Erlangen-Nuremberg initiated an uncontrolled study of patients with intractable rheumatoid arthritis treated with total lymphoid irradiation. Eleven patients (10 females and one male) with an average age of 66 (range 56–75) years were selected jointly with the Institute of Clinical Immunology and Rheumatology of the University. Patients' histories were between 7 and 30 years long, with exacerbations varying in frequency and intensity. At the time of entry into the study, the patients had multiple joint involvement with swelling, synovitis and deformities. The patients were severely restricted in their ability to perform self-care and occupational tasks.

Admittance to the study was contingent upon the patients meeting the same criteria as those applied by the Stanford (Strober et al) and Boston (Trentham et al) groups.

(1) Advanced and intractable disease after unsuccessful long-term therapy using non-steroidal anti-rheumatic drugs, chloroquine derivatives, D-penicillamine and gold salts Some patients had already been subjected to chemotherapy without benefit.

(2) Patients suffering from classic rheumatoid arthritis as defined by the criteria of the American Rheumatism Association (Ropus et al, 1958)

Patients with evidence of visceral organ involvement, bacterial infections, anaemia, leucopenia and thrombocytopenia were not included. Patients younger than 50 years were not entered into the study. Further criteria of exclusion were impaired general health and severe chronic diseases such as tuberculosis and congestive heart failure.

Prior to radiotherapy, the patients underwent a precise clinical and rheumatological examination. Apart from general laboratory investigations, including a differential blood count and serology, analysis of immune complexes was carried out. Peripheral blood lymphocyte subpopulations were determined with monoclonal antibodies Additionally, the *in-vitro* functions of the lymphocytes were studied by the lymphocyte transformation test after stimulation with mitogens. All examinations were repeated during and after therapy for a period of up to 18 months. The following list gives the separate clinical, laboratory and immunological examinations.

Clinical:	frequency of exacerbations, number of joints involved, drug consumption, self-care index, morning stiffness, joint swelling, joint mobility.
Laboratory:	erythrocyte sedimentation rate (ESR), serological tests of the liver (SGOT, SGPT, gamma GT, bilirubin) and kidney (urea, uric acid, creatinine, electrolytes), alkaline phosphatase, thyroid function tests (T3, T4), blood count and differential blood count.
Immunology:	Rose-Waaler test, absolute lymphocyte count, T cells and their subpopulations (T-helper cells, T-suppressor cells), B cells and circulating immune complexes

Irradiation technique

Total lymphoid irradiation was delivered by the technique described by Kaplan (1980a) for the treatment of Hodgkin's disease with a 6 MV or 10 MV linear accelerator. At first, the supradiaphragmatic lymph nodes were irradiated with the "mantle field" including cervical, axillary, mediastinal and hilar lymph nodes in fractions of 2 Gy to a total dose of 20 Gy in 2 weeks Without interruption, treatment was then given to lymphoid tissue below the diaphragm by an "inverted Y" field (para-aortic, iliac and inguinal lymph nodes), which included the spleen, with the same fractionation scheme and total dose. Treatment was usually given five times per week.

Clinical assessment

Clinical disease activity was assessed on the basis of the activity index (Ropus et al, 1985) established by the American Rheumatism Association. This index covers duration of morning stiffness, extent of joint swelling, number of joints involved, and such laboratory parameters as ESR and haemoglobin levels. The maximum total score attainable is 30 points.

RESULTS

The success of total lymphoid irradiation was assessed on the basis of clinical, laboratory and immunological examinations, comparing the parameters before treatment with those after therapy Out of 11 patients, nine could be followed up for 6 months, six for 1 year and three for 18 months.

Of nine patients followed up, the activity index rose in two, remained static in three, and dropped in four (Fig. 1). Two months after radiotherapy, the index fell in all patients. The higher value shown in Case 3 after 18 months is probably attributable to a renewed increase in ESR, although clinically no reactivation of rheumatoid arthritis was observed.

At the same time the daily dose of cortisone and anti-inflammatory drugs could be reduced. Of the laboratory parameters, the ESR proved to be very sensitive, and correlated best with the clinical course of rheumatoid arthritis. Elevated pre-treatment values dropped in the course of the first 6 months in seven out of nine patients after irradiation, without returning to within the normal range (Fig. 2). In three patients, the ESR increased after 18 months in the absence of any clinical correlate. The significance of this remains unclear.

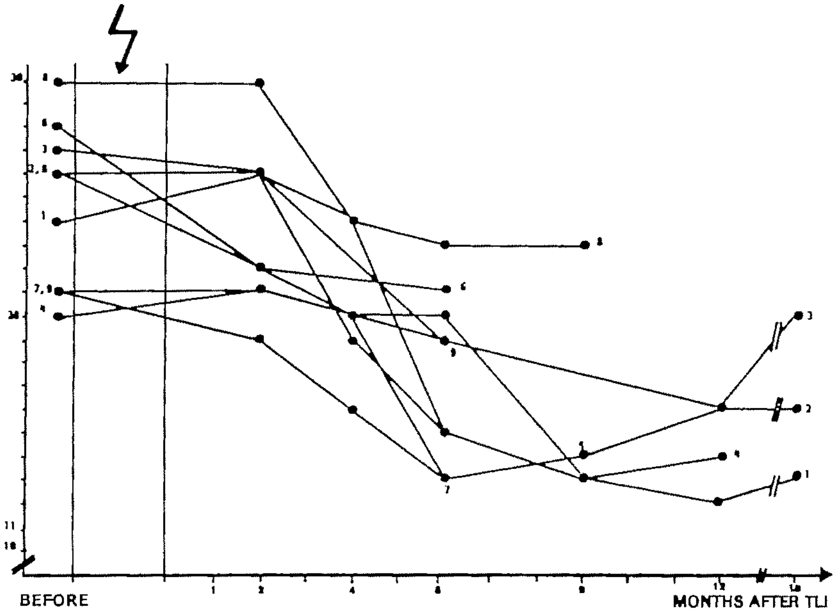

FIG. 1.
Changes in the activity index after total lymphoid irradiation. The figure shows the evaluated data from nine patients.

Of the serological tests, rheumatoid factors (Latex-Rose-Waaler test), liver parameters (SGPT, SGOT, gamma GT, bilirubin), kidney serology (urea, uric acid, creatinine, electrolytes), alkaline phosphatase, serum and immunoelectrophoresis, as well as the thyroid function parameters, remained unchanged. The haemoglobin level alone showed an increase.

To assess the immune reaction, peripheral-blood lymphocytes and their subpopulations (T-helper cells and T-suppressor cells) were studied with monoclonal antibodies and the rosette technique. During radiotherapy, the absolute lymphocyte count dropped in all patients by roughly one half, to return again to the original levels after treatment. In contrast, the T lymphocytes increased again only slightly after the therapy-induced drop. The T-helper cells also decreased to about half their original number, and continued to decrease during follow-up. The T-suppressor cells remained unchanged during therapy and during follow-up. Thus, the T-helper cell: T-suppressor cell ratio dropped from 2 : 1 to 1 : 1, due mainly to the reduction in T-helper cells (Fig. 3).

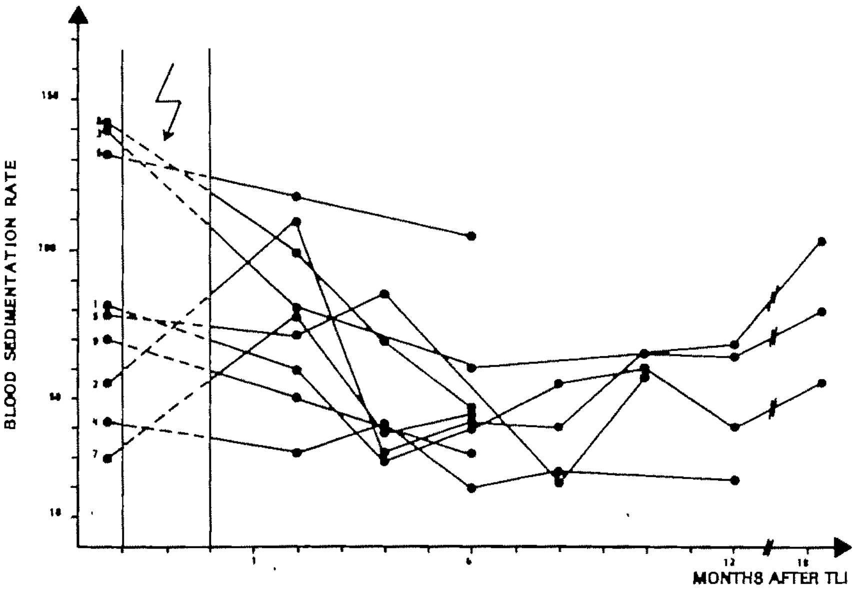

FIG. 2.
Changes in ESR after total lymphoid irradiation in nine patients

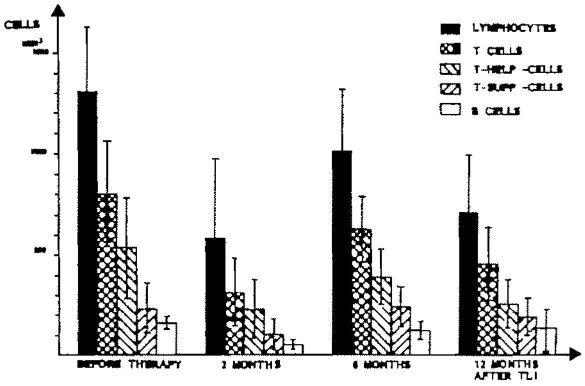

FIG 3.

Changes in the absolute lymphocyte count, T cells, T-helper cells, T-suppressor cells and B cells in the peripheral blood after total lymphoid irradiation (TLI) Error bars show ±1 SD.

Side-effects and complications

Treatment was well tolerated Fatigue, lassitude and nausea were observed after irradiation, and were more pronounced than in patients with Hodgkin's disease. They were, however, transient, and the patients recovered shortly after completion of treatment.

Four of 11 patients died. In a female patient, haemorrhage of a recurrent duodenal ulcer, occurring after "mantle field" irradiation, made hospitalisation necessary She died 3 months later of renal failure caused by amyloidosis before irradiation to the infradiaphragmatic lymph nodes could be given. Another female patient required cholecystectomy and gastrostomy to treat a gallstone perforation. After successful surgery, the patient, who also had amyloidosis, died in a cardiogenic shock. This happened 2 years after total lymphoid irradiation. A third female patient developed an ulcer and had an acute gastric haemorrhage. During hospitalisation she developed an ulcer in the coccygeal region. An infection of the ulcer caused sepsis resulting in joint empyema that did not respond to antibiotic treatment. She finally died of left heart failure. The fourth patient had to be operated on for Kaposi's sarcoma. Post-operatively, the patient developed a wound infection and an abscess which responded well to antibiotic therapy and drainage. Three months later the patient died of left heart failure.

One patient developed bacterial joint infection in one shoulder and in one prosthetic knee. The infection was treated successfully.

DISCUSSION

In a non-randomised study, 11 patients with intractable rheumatoid arthritis were subjected to total lymphoid irradiation after unsuccessful basic therapy. In four patients the clinical symptoms improved during treatment. Two months after completion of treatment, symptoms had improved in all patients. The frequency of exacerbations had decreased, as had the number of joints involved. Morning stiffness, tenderness and swelling subsided and stabilised after 6 months, with an improvement in mobility. The consumption of analgesics and steroids also decreased.

To date, in three patients the clinical improvement has remained static for more than 2 years.

Total lymphoid irradiation was applied as described by the Stanford group. We used a dose of up to 20 Gy (5 × 2 Gy per week) (Stanford: 4 × 1.5–2.2 Gy) administered without interruption via the "mantle field" and "inverted Y" within 4 weeks. The treatment time used by the Stanford group was 5–6 weeks. In contrast, the Boston group delivered a total dose of 30 Gy via the "mantle field", a para-aortic field including the spleen and a pelvic lymph node field. Two-week intervals were observed between the series.

The immunosuppressive effect achieved by the two groups was identical using 20 Gy and 30 Gy. Since the two patient groups were not identical, it is impossible to determine whether or not the patients receiving a dose of 30 Gy had a higher level of morbidity during the observation period compared with the patients treated with only 20 Gy.

The general side-effects of radiotherapy in our patients were fatigue, lassitude and nausea, which were transient and tolerable. Two female patients died 3 months and 2 years after completion of treatment, one of renal failure due to amyloidosis The other had an operation for a gallstone perforation and died in cardiac shock with underlying amyloidosis. Without the relevant experience, the question as to whether this mortality was an indirect consequence of radiotherapy remains unanswered. The third patient died of left heart failure with underlying diabetes mellitus, cachexia, coccygeal ulcer and unresponsive sepsis leading to joint empyema The fourth female patient died of left heart failure 3 months after removal of a Kaposi's sarcoma complicated by wound infection and joint empyema which responded to antibiotics.

Another female patient developed shoulder- and knee-joint empyema at 4 and 26 months after total lymphoid irradiation, but responded well to antibiotics.

The high mortality rate prompts a reconsideration of the value of total lymphoid irradiation and the indication for it, and the establishment of more stringent patient selection criteria. Also, this therapy requires close follow-up of the patients, who must be informed about their weakened immune defences and increased susceptibility to infections, in order to avoid such incidents.

In all patients the absolute lymphocyte count dropped during and after therapy. While the percentage of T cells dropped, that of the B cells increased. Suppression of T lymphocytes with a reduction in T-helper cells, with T-suppressor cell levels remaining unchanged, reflects a modification in immunoreactivity after total lymphoid irradiation. In some patients, this cell-bound immunosuppression persisted for up to 18 months. Similar observations were made by the Stanford and Boston groups.

Our results of a long-term immunosuppression after total lymphoid irradiation for advanced and intractable rheumatoid arthritis correspond to those of Strober et al (1981, 1983) and Trentham et al (1981). During and after treatment, a lasting improvement in clinical symptoms and the quality of life is seen. Nevertheless, total lymphoid irradiation of rheumatoid arthritis is still experimental. Randomised studies involving larger numbers of patients and critical patient selection are required in order to avoid increased morbidity and mortality after successful irradiation.

REFERENCES

BRAHN, E., HELFGOTT, S. M., BELLI, J. A., ANDERSON, R. J., REINHERZ, E. L., SCHLOSSMAN, S. F., AUSTEN, K. F. & TRENTHAM, D. E., 1984. Total lymphoid irradiation therapy in refractory rheumatoid arthritis. Fifteen-to-forty-month follow up. *Arthritis and Rheumatology*, *27*, 481–488.

BOBROVE, A. M., FUKS, Z., STROBER, S. & KAPLAN, H., 1975. Quantification of T and B lymphocytes and cellular immune function of Hodgkin's disease. *Cancer*, *36*, 169–179.

FIELD, E. H., STROBER, S., HOPPE, R. T., CALIN, A., ENGLEMAN, E. G., KOTZIN, B. L., TANAY, A. S., CALIN, H. J., TERRELL, C. P. & KAPLAN, H. S., 1983. Sustained improvement of intractable rheumatoid arthritis after total lymphoid irradiation. *Arthritis and Rheumatism*, *26*, 937–946.

FUKS, Z., STROBER, S., BOBROVE, A. M., SASAZUKI, T., MCMICHAEL, A. & KAPLAN, H. S., 1976. Long-term effects of radiation on T and B lymphocytes in peripheral blood of patients with Hodgkin's disease. *Journal of Clinical Investigation*, *48*, 803.

GOTTLIEB, M., STROBER, S., HOPPE, R. T., CRUMET, F. C. & KAPLAN, H. S., 1980. Engraftment of allogenic bone marrow without graft vs host disease in mongrel dogs using total lymphoid irradiation. *Transplant*, *29*, 487–492.

KAPLAN, H. S., 1980a. Hodgkin's disease: unfolding concepts concerning its nature, management and prognosis. *Cancer*, *45*, 2439–2474.

——1980b. *Hodgkin's Disease*. 2nd edit. (Harvard University Press, Cambridge, Mass.) pp. 336–441.

KOTZIN, B. L. & STROBER, S. D., 1979. Reversal of NZB/NZW disease with total lymphoid irradiation. *Journal of Experimental Medicine*, *150*, 371–378.

KOTZIN, B. L., STROBER, S., ENGLEMAN, E. G., CALIN, A., HOPPE, R. T., KANSAS, G. S., TERRELL, C. P. & KAPLAN, H. S., 1981. Treatment of intractable rheumatoid arthritis with total lymphoid irradiation. *New England Journal of Medicine*, *305*, 969–975.

ROPUS, M. W., BENNETT, G. A., COBB, S., JACOX, R. & JESSOR, R. A., 1958. 1958 revision of diagnostic criteria for rheumatoid arthritis. *Bulletin on Rheumatic Diseases*, *9*, 175–176.

SCHURMANN, D. J., HIRSHMAN, H. P. & STROBER, S., 1981. Total lymphoid and local joint irradiation in the treatment of adjuvant arthritis. *Arthritis and Rheumatology*, *24*, 38–44.

SLAVIN, S., STROBER, S., FUKS, Z. & KAPLAN, H. S., 1976. Long term survival of skin allografts in mice treated with fractionated total lymphoid irradiation. *Science*, *1983*, 1252–1254.

STROBER, S., FIELD, E. M., KOTZIN, B. L., HOPPE, R. T., ENGLEMAN, E. L., TANAY, A. S. & KAPLAN, H. S., 1983. Treatment of rheumatoid arthritis with total lymphoid irradiation (TLI): immunological and clinical changes. *Radiotherapy and Oncology*, *1*, 43–52.

STROBER, S., KOTZIN, B. L., HOPPE, R. T., SLAVIN, S., GOTTLIEB, M., CALIN, A., FUKS, Z. & KAPLAN, H., 1981. The treatment of intractable rheumatoid arthritis with lymphoid irradiation. *International Journal of Radiation Oncology, Biology, Physics*, *7*, 1–7.

TRENTHAM, D. E., BELLI, J. A., ANDERSON, R. J., BUCKLEY, J. A., GOETZEL, E. J., DAVID, J. R. & AUSTEN, K. F., 1981. Clinical and immunologic effects of fractionated total lymphoid irradiation in refractory rheumatoid arthritis. *New England Journal of Medicine*, *7*, 976–982.

TWOMEY, J. J. & RICE, L., 1980. Impact of Hodgkin's disease upon the immune system. *Seminars in Oncology*, *7*, 114–125.

Book review

The Radiobiology of Radium and Thorotrast Ed. by W. Gössner, G B Gerber, U Hagen and A Luz, pp 210, 1986 (Urban and Schwarzenberg, Munich, Wien, Baltimore), DM 118.
ISBN 3-541-70511-6 (Munich)
0-8067-0511-6 (Baltimore)

This book reports the 38 papers given at a symposium held at Neuherberg in 1984 It is important because it contains the latest and most comprehensive statement on the effects on man of radioactivity incorporated in his body: ^{226}Ra and ^{228}Ra in the so-called "radium-poisoning" cases in the USA and some in the UK, ^{224}Ra in German patients treated for ankylosing spondylitis, and ^{232}Th in "Thorotrast" cases in Germany, Denmark, Japan and the USA.

The book opens with a review paper by Mole on leukaemia induction in man by radionuclides, which includes data on the above radionuclides together with some on low linear energy transfer radiations, as well as on external irradiation with X rays, γ rays and neutrons The second paper, by Rundo and his colleagues, is a comprehensive summary of the data available on radium cases in the USA, now totalling over 5000. The third paper, by Baverstock and Papworth, deals with the much smaller number, about 1000, of UK radium luminisers. The next six papers, by Spiess, Mays, Gössner and their co-workers, give the full present picture of the work on the 899 German ^{224}Ra cases, including data on growth retardation, cataracts and tooth breakage as well as on bone tumours and haemopoietic effects. There are eight papers on Thorotrast studies, showing a renewed interest in the late effects of the use of this radiological contrast medium since the early Danish studies by Faber, and some retrospectively study considerable numbers of cases.

Almost half the total number of papers cover miscellaneous topics, many involving animals, which are, nevertheless, relevant to the study of radium and thorium in humans, especially in bone These papers include investigations of the distribution and metabolism of bone-seeking radionuclides and their dosimetry

The book is essentially for the expert, for whom it contains a wealth of information. It is of considerable interest, however, to all those concerned with the effects of ionising radiations on man, because of the factual information it contains on the only groups of human beings known to have suffered deleterious effects of internally absorbed radionuclides It will be a valuable addition to the radiation literature of many departmental libraries and of personal interest to the specialist studying the bone-seeking radionuclides.

F W SPIERS

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The composition of body tissues

By H. Q. Woodard, Ph.D. and *D. R. White, Ph.D.

Department of Biophysics, Memorial Sloan-Kettering Cancer Center, 1275 York Avenue, New York, NY 10021, USA, and *Radiation Physics Department, St Bartholomew's Hospital, London EC1A 7BE

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ABSTRACT

A reassessment of the composition data given by ICRP (1975) has been completed, augmented with results from appropriate recent studies. The water, lipid, protein, carbohydrate and ash contents, together with elemental compositions, mass and electron densities are given here for 56 body tissues. Seven tissues (adipose tissue, heart, kidney, liver, mammary gland, muscle—skeletal and skin) had sufficient measured data to enable the spread in the results to be evaluated. All the compositions presented apply to healthy, adult humans, except for some new material on the bones of children.

The need for reliable composition and density data of body tissues is a prerequisite in theoretical dosimetry involving radiation interactions in humans. Such data are also essential if realistic tissue substitutes are to be formulated for radiation measurements with phantoms. In both instances, uncertainties in the elemental compositions and mass densities of the body tissues under investigation will lead to reduced confidence in the relevance of the calculated and measured doses.

Uncertainties in the elemental composition of a body tissue may affect the dosimetry of low- and high-energy photon and particulate radiations. The concentrations of high-atomic-number elements ($Z \geqslant 8$) in a tissue will strongly influence photoelectric absorption, while hydrogen content will affect Compton scattering. Differences in mass attenuation coefficients in excess of 10% have been reported between soft tissues (White & Fitzgerald, 1977). In fast-neutron dosimetry the importance of hydrogen is well established, with a 1% deviation in the total hydrogen content of soft tissue producing a 10% change in kerma (International Commission on Radiation Units and Measurements (ICRU), 1977).

The importance of reliable body tissue compositions in radiation dosimetry was realised over 20 years ago, when ICRU (1964) published elemental data for striated muscle and compact bone. These compositions have been widely used, especially the former, which is often referred to as "ICRU muscle". In 1975, the International Commission on Radiological Protection (ICRP) published, in a report on "Reference Man", comprehensive elemental data on over 80 organs, tissues and tissue components (ICRP, 1975). Unfortunately, errors and inconsistencies exist within these data; for example, over 20% of the compositions quoted had mass discrepancies exceeding 5% (White & Fitzgerald, 1977).

The elemental composition of a body tissue is dependent upon the relative amounts and compositions of the various substances (water, lipid, protein, carbohydrate, minerals) which make up the tissue. The literature reveals significant variations between normal persons in the composition of certain body tissues (adipose tissue, heart, kidney, liver, muscle—skeletal, skin). Conversely, some body tissues (cortical bone, erythrocytes) exhibit small variations between individuals.

In this study, three sources of composition data have been considered. Firstly, the published analyses quoted in Reference Man have been reassessed in order to eliminate anomalies. Secondly, computer-assisted searches of the literature covering the period 1966–85 yielded a surprisingly small number of additional useful data. Thirdly, these results were supplemented by unpublished measurements undertaken on selected body tissues during the past 30 years by one of the authors (H Q W.).

Collating data from different authors has its problems as the tissue specimens may be handled in different ways. In particular, some use fresh tissue, others use material which is dehydrated, defatted or otherwise manipulated. Considerable effort has been made in this study to detect and correct such irregularities in order to obtain a reliable and consistent set of results.

Results for 56 body tissues are presented here. Whenever sufficient data are available, the results for tissues known to vary between individuals are quoted as mean ± 1 standard deviation. Single compositions are given for the remaining tissues. Mass and electron densities are tabulated for all of the body tissues analysed.

Unless otherwise specified, the compositions presented in this paper apply to *healthy, adult humans*

MATERIALS AND METHODS

Before the analytical techniques used in this study are discussed, it is important to describe clearly the selected body tissues, as much confusion has been caused in the past by ambiguous descriptions. Sources of composition data will be given at the end of each brief descriptive passage.

Adipose tissue

This is composed of a protein matrix supporting cells (adipocytes) highly specialised for the storage of lipid, which is a mixture of the triglycerides of various long-

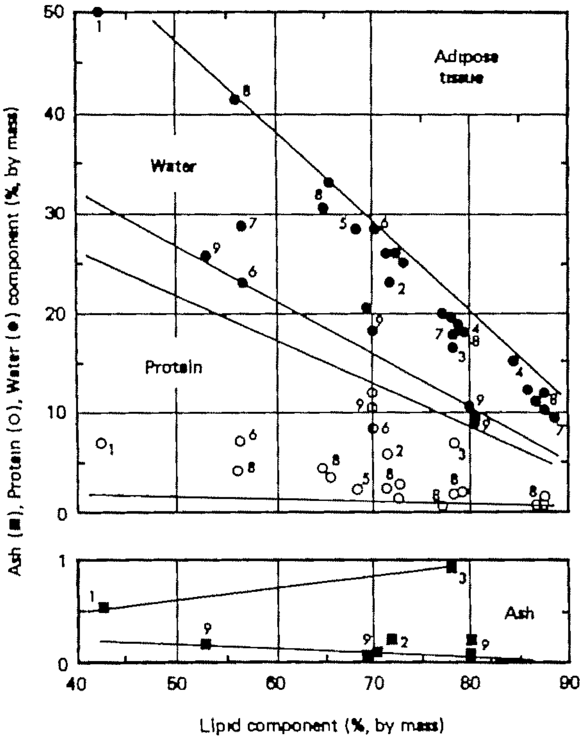

FIG. 1

Plots of lipid components versus ash, protein and water components for adipose tissue Plotted data: 1, Mitchell et al, 1945, 2, Forbes et al, 1953, 3, Forbes et al, 1956; 4, Entenmen et al, 1958; 5, Pawan & Clode, 1960; 6, Thomas, 1962; 7, Morse & Soeldner, 1963; 8, Baker, 1969, 9, Woodard, 1986.

chain fatty acids. Adipose tissue, often erroneously referred to as "fat", makes up some 18% and 29% by mass in the male and female, respectively Data from nine sources are shown graphically in Fig. 1. (Additional information was obtained from. Keys & Brožek, 1953; Dju et al, 1958; Morse & Soeldner, 1965; Martinsson, 1967.)

Adrenal gland

These two small endocrine glands are just above and attached to the kidneys. The tissue of medulla produces adrenalin; that of the cortex produces several steroid hormones. No distinction is made here in the composition of these two tissues. Available data are sparse (Dju et al, 1958, Long et al, 1961; Tipton & Cook, 1963; Slater et al, 1964; Eisenstein, 1967)

Aorta

This major artery in the body is a contractile, muscular tissue, important radiologically because it often develops calcified plaques in the intima. Available composition data are again sparse (Kirk, 1962; Tipton & Cook, 1963, Woodard, 1986).

Blood

The composition of *erythrocytes*, the major formed elements in the blood, varies little with health *Plasma*, the non-cellular element in circulating blood, normally contains 6.2–7.8%, by mass, of protein and numerous electrolytes whose concentrations are kept nearly constant by powerful homeostatic mechanisms. The composition is dominated by the high water content. *Whole blood* was assumed to comprise 45% erythrocytes and 55% plasma, by volume (Neufeld, 1937, Albritton, 1952; Houssay et al, 1955; Altman & Dittmer, 1961; Long et al, 1961; Oser, 1965, Wintrobe, 1967; Tandon et al, 1978; Wootton & Freeman, 1982).

Brain

Cerebrospinal fluid bathes the neurological structures in the brain and spinal cord. It is not an ultrafiltrate of plasma but is a special secretion. There are two types of tissue in the brain. *White matter* contains much more lipid than *grey matter*. The lipids are the most distinctive constituents and are of several types. Some of these are present in combinations with proteins or carbohydrates and are not always distinguished in chemical analyses, resulting in variations of up to 10% in reported lipid content. In this work it has been assumed that the lipids of the brain were (by mass) 50% sphingomyelin, 25% cerebroside and 25% cholesterol (Fieser & Fieser, 1963). Data from seven sources were used (Himwich & Himwich, 1957; McIlwain, 1959; Altman & Dittmer, 1961; Long et al, 1961; Diem, 1962; Widdowson & Dickerson, 1964; Fillerup & Mead, 1967)

Connective tissue

This is made up of tendons, fascia and periarticular tissue. As information on humans is lacking, the composition adopted was based on the tendons of cattle (Oser, 1965).

Eye lens

The transparent, biconvex, semisolid body in the eye does not have a blood supply. The mass density increases with age and a value appropriate for a 40-year-old was accepted (Scammon & Hesdorffer, 1937, Spector, 1956; Long et al, 1961).

Gallbladder

In the absence of any definitive information, the *wall* of the gallbladder was assumed to be the same as muscle—skeletal. The secretion *bile* has a high water content, with small quantities of cholic acid and mucin (Oser, 1965).

Gastrointestinal tract

Intestinal wall, oesophagus and *stomach* were considered. The composition of the oesophagus, a muscular tube extending from the pharynx to the stomach, was assumed to be the same as that for muscle—skeletal. The intestinal wall and the stomach have similar compositions, with the rapidly metabolising intestines containing a higher proportion of water but a lower protein content (Neufeld, 1937; Mitchell et al, 1945; Forbes et al, 1953, 1956; Tipton & Cook, 1963; Eve, 1966; Saunders et al, 1966)

Heart

The published data for the mass of heart muscle and the volume of blood before contraction are variable. It is well known that cardiac output and size change markedly with activity in healthy individuals and the baseline values are altered in disease. Compositions for the heart with and without blood were derived, assuming that the blood-filled heart comprises (by mass) 40% heart tissue and 60% whole blood (Mitchell et al, 1945; Friedman, 1951; Forbes et al, 1953, 1956; Spector, 1956; Dju et al, 1958; Dittmer & Grebe, 1959; Widdowson & Dickerson, 1960, 1964; Tipton & Cook, 1963).

Kidney

The kidney is composed of two types of tissue, the cortex and the medulla, which have different metabolic functions The considerable volume in the central part of the organ is occupied by collecting ducts. The data reported here are average values for the cortex and medulla *without* the ducts (Neufeld, 1937; Mitchell et al, 1945; Forbes et al, 1953, 1956; Spector, 1956; Long et al, 1961; Diem, 1962; Tipton & Cook, 1963).

Liver

This large organ, which is made up of several cell types, has multiple functions. It takes up simple compounds from the blood and the chyle and synthesises albumin and complex lipids. These products are stored temporarily and then released into the circulation. Hence, the protein and lipid content of the liver is higher a few hours after a meal than after a fast. In disease, either the protein or the lipid content may increase. These conditions probably account for much of the variability in the reported liver compositions. Composition data were available from 14 sources (Neufeld, 1937, Mitchell et al, 1945, Hildes et al, 1949; Widdowson et al, 1951; Forbes et al, 1953, 1956; Spector, 1956; Dju et al, 1958; Widdowson & Dickerson, 1964; Long et al, 1961; Diem, 1962; Tipton & Cook, 1963; Jorulf, 1975; Ikawa et al, 1983)

Lung

At any time during life nearly half of the mass of a lung is made up of blood circulating in the vessels. The average composition of lung tissue, *parenchyma*, is very similar to that of whole blood, but the distribution of radionuclides in the two substances may be very different. Hence, the compositions of *lung parenchyma* and *lung—blood-filled* are listed separately here. The composition of the latter is taken to be, by mass, 57% parenchyma and 43% whole blood. The considerable variation in water content due to disease probably contributes to the spread in the published compositions for this organ (Neufeld, 1937; Mitchell et al, 1945; Forbes et al, 1953, 1956; Cander & Forster, 1959; Fowler & Young, 1959; Diem, 1962; Tipton & Cook, 1963; Widdowson & Dickerson, 1964).

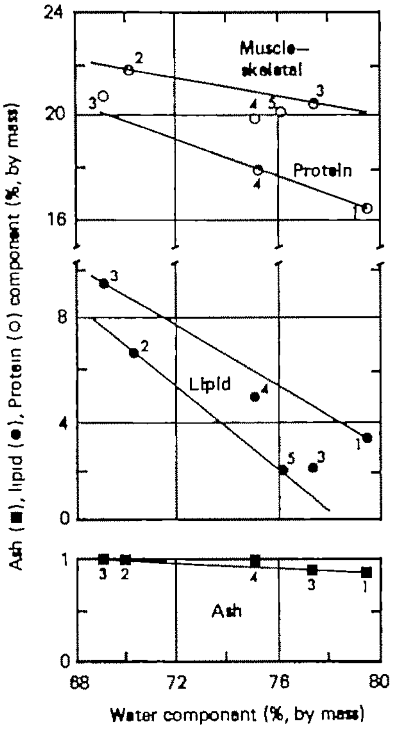

FIG. 2.

Plots of water components versus ash, lipid and protein components for muscle—skeletal Plotted data: 1, Mitchell et al, 1945, 2, Forbes et al, 1953, 3, Forbes et al, 1956; 4, McIlwain, 1959; 5, Fomon, 1966

Lymph

Described as "blood without its red corpuscles" (Oser, 1965), the composition adopted for blood plasma was used.

Mammary gland

These glands are embedded in, but separate from, a large mass of hormonally controlled adipose tissue. The glands themselves contain considerable specialised lipid. The data here are the means of seven specimens from post-menopausal women. No data are available from lactating glands (Hammerstein et al, 1979; Woodard, 1986).

Muscle—skeletal

Skeletal or striated muscle comprises (by mass) approximately 40% of the normal adult male and 30% of the female. The tissue consists primarily of specialised contractile cells, but also contains variable amounts of fascia and other connective structures, blood vessels, lipid and interstitial fluid. The amounts of these secondary components relative to the contractile cells may vary considerably, even in health. Composition data from five sources are shown graphically in Fig. 2 (Additional information was obtained from: Neufeld, 1937; Hildes et al, 1949; Dju et al, 1958; Diem, 1962; Tipton & Cook, 1963; Widdowson & Dickerson, 1964.)

Ovary

Compositions from five published sources were considered for this female reproductive organ (Neufeld, 1937; Block, 1951; Spector, 1956; Long et al, 1961; Tipton & Cook, 1963).

Pancreas

This is a large endocrine gland whose main function is the production of insulin (Neufeld, 1937; Mitchell et al, 1945; Forbes et al, 1953; Tipton & Cook, 1963).

Prostate

This is the main source of seminal fluid in the male; it has a tendency to hypertrophy in later life and may reach 2–3 times its normal volume (Spector, 1956, Tipton & Cook, 1963).

Skeleton

The principal components of the skeleton, namely *cartilage, cortical bone, red* and *yellow marrow* and *spongiosa*, were reviewed recently by the authors (Woodard & White, 1982). The compositions given in the review have been updated here in the light of further investigations (Woodard, 1986).

Skin

The skin is composed of two distinct layers, the epidermis and the dermis, together with an ill-defined connective-tissue layer, the hypodermis, which blends into the adipose tissue. The layers are difficult to separate and each varies with age, sex and race and between different parts of the body of the same person. The difficulty of separating the layers, together with the variability between individuals, contribute to the wide range of reported compositions (Mitchell et al, 1945; Forbes et al, 1953, 1956, Rothman, 1954; Spector, 1956, Diem, 1962; Tipton & Cook, 1963; Widdowson & Dickerson, 1964; Brincat et al, 1983; Woodard, 1986).

Spleen

The size and composition of the spleen, which in the healthy adult stores, recycles or destroys erythrocytes, varies with its physiological activity (Neufeld, 1937; Widdowson et al, 1951; Forbes et al, 1953, 1956; Spector, 1956, Diem, 1962; Tipton & Cook, 1963).

Testis

Composition data are sparse for this male reproductive organ (Neufeld, 1937; Tipton & Cook, 1963).

Thyroid

This gland, whose main function is the elaboration of the hormones triiodothyronine and tetraiodothyronine, contains considerable deposits of the specialised protein, thyroglobulin. Where intake of iodine is deficient, the gland may increase to many times its normal mass (Neufeld, 1937; Shohl, 1939; Long et al, 1961; Tipton & Cook, 1963; Widdowson & Dickerson, 1964; Goldberg et al, 1968).

Trachea

This major airway contains rings of cartilage whose function is to keep it open, alternating with muscle and connective tissue. In the absence of reliable data, the trachea was assumed to be composed of 90% muscle—skeletal and 10% cartilage, by mass.

Urinary bladder

This muscular sac lined with mucosa acts as a reservoir for urine. It is highly distensible, with its volume varying typically from 30 cm^3 to 220 cm^3. The *wall* of the bladder was taken to be the same as muscle—skeletal. *Urine* is predominantly water, with small quantities of urea and other electrolytes (Oser, 1965). Published values for mass, volume and wall thickness were not self-consistent. Hence, from an estimate of the bladder contents in intravenous pyelograms in which the bladders appeared normal, a mean wall mass of 60 g was established and urine volumes of 33.5 ml and 212 ml for the contracted and distended bladder, respectively. From these data the elemental compositions of the empty and filled bladder were derived.

In addition to the references cited for these body tissue compositions, note has been taken of the interpretations given by ICRP (1975) and the information reported by Kerr (1982).

For each body tissue the analytical procedure adopted for arriving at a satisfactory composition was as follows:

(i) A set of data was compiled for the contents ($\geqslant 0.1\%$ by mass) of water, lipid, protein, carbohydrate, ash or other components in the given body tissue.
(ii) Similarly, the concentrations ($\geqslant 0.1\%$ by mass) of elements with $Z > 8$ were compiled.
(iii) Data obviously from diseased tissues or those derived from paediatric sources were eliminated.
(iv) For more than five sets of reliable data, the co-relationships between different components were derived graphically (Figs 1, 2). This is illustrated for adipose tissue and muscle—skeletal. This enabled three sets of compositions to be calculated once the mean (M) and standard deviation (σ) were established, that is the compositions appropriate to $M-\sigma$, M and $M+\sigma$.
(v) For all other sets of data, only a single (mean) composition was established.

(vi) The derived composition was corrected to 100% mass by allocating any missing mass to the major ($\geqslant 75\%$) component, or proportionally between two major components when each were $< 75\%$. Excess mass was corrected in the same fashion. Generally, these corrections were within the reported variations in the major component(s).

(vii) The elemental composition was then calculated from the elemental compositions of the components. Minor rounding errors were generally no more than 0.1% by mass and were attributed to the major component.

(viii) The mass density was derived from the mass proportions and mass densities of the components (Fomon, 1966). This value was usually within 2% of the mean mass density derived from published measured values.

(ix) Mass and volume electron densities (el.kg^{-1} and el.m^{-3}) were then calculated from the elemental atomic weights, Avogadro's number (6.022045×10^{26} kmol^{-1}) (Handbook of Chemistry and Physics, 1982) and the accepted mass density of the body tissue.

Results

The results of the analyses are given in Tables I–III

The amounts (%, by mass) of water, lipid, protein and other components in each body tissue are listed in Table I. Certain components, such as the carbohydrate chondroitin sulphate, the lipid sphingomyelin and protein, contain elements with $Z > 8$. The remaining high-atomic-number elements that have been reported are included as "minerals" in parentheses beside the ash content in the sixth column of Table I. These values are often less than the ash contents.

Whenever the available data for a body tissue permitted the spread in the compositions to be calculated, the resulting three compositions are presented as Nos 1, 2, 3, referring to values derived from $M-\sigma$, M and $M+\sigma$, respectively.

The elemental compositions of the body tissue components are given in Table II. Three types of carbohydrate (chondroitin sulphate, monosaccharide and polysaccharide) and four types of lipid (cerebroside, cholesterol, glycerol trioleate and sphingomyelin) have been used.

Table III lists the elemental composition (%, by mass), mass density, volume and mass electron densities of each body tissue. Gallbladder wall, gastrointestinal tract—oesophagus and urinary bladder wall are not included as the composition of muscle—skeletal was accepted as being representative of these tissues. Lymph is also omitted from the table because of its similarity to blood plasma.

Discussion

The tabulated elemental data given here for body tissues represent a reassessment and updating of the

TABLE I

Water, lipid, protein and ash components of the body tissues considered in this study

Body tissue	Percentage by mass				
	Water	Lipid	Protein	Other	Ash (minerals*)
Adipose tissue 1	30.5	61.4	7.9	—	0.3 (0.2)
Adipose tissue 2	21.2	74.1	4.4	—	0.3 (0.3)
Adipose tissue 3	11.4	87.3	1.0	—	0.3 (0.3)
Adrenal gland	58.1	26.0	15.5	—	0.5 (0.4)
Aorta	72.1	1.8	25.0		1.4 (1.1)
Blood—erythrocytes	64.0	0.5	34.7	0.1 (monosaccharide)	1.1 (0.7)
Blood—plasma	91.9	0.7	6.6	0.1 (monosaccharide)	1.0 (0.7)
Blood—whole	79.0	0.6	19.6	0.1 (monosaccharide)	0.9 (0.7)
Brain—cerebrospinal fluid	99.0	—	—	0.1 (monosaccharide)	0.9 (0.9)
Brain—grey matter	82.6	5.3†	10.0	1.0 (monosaccharide)	1.5 (1.1)
Brain—white matter	68.5	18.1†	11.5	1.0 (monosaccharide)	1.4 (0.9)
Connective tissue	60.4	1.0	36.6	0.9 (monosaccharide)	1.3 (1.1)
Eye lens	64.1	2.0	33.6	—	0.4 (0.3)
Gallbladder—wall		As muscle—skeletal			
Gallbladder—bile	88.4	0.9	0.4	5.4 (cholic acid) 4.1 (mucin)	0.9 (0.8)

TABLE I—*continued*

Body tissue	Percentage by mass				
	Water	Lipid	Protein	Other	Ash (minerals*)
GI tract—small intestine (wall)	80.6	5.9	13.0	—	0.7 (0.5)
GI tract—oesophagus	As muscle—skeletal				
GI tract—stomach	76.3	6.2	17.0	—	0.8 (0.5)
Heart 1	71.0	10.0	18.2	—	0.9 (0.8)
Heart 2	75.9	6.2	17.1	—	0.9 (0.8)
Heart 3	80.9	2.4	15.9	—	0.9 (0.8)
Heart—blood-filled	77.7	2.8	18.6	0.1 (monosaccharide)	0.9 (0.8)
Kidney 1	72.3	6.9	19.9		0.9 (0.9)
Kidney 2	76.6	4.8	17.7		0.9 (0.9)
Kidney 3	80.5	2.8	15.8		0.9 (0.9)
Liver 1	72.8	7.8	16.1	2.2 (polysaccharide)	1.2 (1.1)
Liver 2	74.5	4.6	17.6	2.2 (polysaccharide)	1.2 (1.1)
Liver 3	75.6	1.5	19.6	2.2 (polysaccharide)	1.2 (1.1)
Lung—parenchyma	80.6	1.3	17.1	—	1.1 (1.0)
Lung—blood filled	79.8	1.0	18.2	—	1.0 (1.0)
Lymph	As blood—plasma				
Mammary gland 1	30.2	56.2	13.3	—	0.4 (0.3)
Mammary gland 2	51.4	30.9	17.4	—	0.4 (0.3)
Mammary gland 3	72.6	5.6	21.5	—	0.4 (0.3)
Muscle—skeletal 1	70.0	6.8	21.3	1.0 (polysaccharide)	1.0 (0.9)
Muscle—skeletal 2	74.1	4.2	19.8	1.0 (polysaccharide)	1.0 (0.9)
Muscle—skeletal 3	78.6	1.6	17.9	1.0 (polysaccharide)	1.0 (0.9)
Ovary	82.8	2.3	14.0	—	1.0 (0.9)
Pancreas	73.3	12.8	13.1	—	1.2 (0.8)
Prostate	83.3	1.2	15.0	—	1.1 (0.5)
Skeleton—cartilage	75.0	—	11.0	11.0 (chondroitin sulphate)	3.0 (3.0)
Skeleton—cortical bone	12.2	—	24.6	5.2 (monosaccharide)	58.0 (58.0)
Skeleton—red marrow	39.7	39.7	20.0	—	0.6 (0.6)
Skeleton—spongiosa	As 33% skeleton—cortical bone+67% marrow, by mass (marrow assumed to be 50% red marrow+50% yellow marrow)				
Skeleton—yellow marrow	15.3	80.4	4.0	—	0.5 (0.3)
Skin 1	58.6	13.5	27.2	—	0.7 (0.7)
Skin 2	65.3	9.4	24.6	—	0.7 (0.7)
Skin 3	72.1	5.2	22.0	—	0.7 (0.7)
Spleen	78.7	1.8	18.6	—	1.3 (0.9)
Testis	82.7	4.5	12.0	—	1.1 (0.8)
Thyroid	78.4	4.4	14.0	2.5 (monosaccharide)	1.1 (0.7)
Trachea	As 90% muscle—skeletal+10% cartilage (by mass)				
Urinary bladder—wall	As muscle—skeletal				
Urinary bladder—urine	96.3	—	—	2.4 (urea)	0.9 (1.3)
Urinary bladder—empty	As 66% muscle—skeletal+34% urine, by mass				
Urinary bladder—filled	As 22% muscle—skeletal+78% urine, by mass				

*Includes remaining elements with $Z > 8$

†Lipid in brain assumed to be 50% sphingomyelin+25% cerebroside+25% cholesterol, by mass.

TABLE II

THE ELEMENTAL COMPOSITIONS OF THE BODY TISSUE COMPONENTS

Component	Elemental composition (% by mass)
Carbohydrate—chondroitin sulphate	H(4.6), C(36.6), N(3.0), O(48.8), S(7.0)
Carbohydrate—monosaccharide	H(6.7), C(40.0), O(53.3)
Carbohydrate—polysaccharide	H(6.2), C(44.5), O(49.3)
Cholic acid	H(9.9), C(70.5), O(19.6)
Lipid—cerebroside	H(9.8), C(63.5), N(3.0), O(23.7)
Lipid—cholesterol	H(12.0), C(83.9), O(4.1)
Lipid—glycerol trioleate	H(11.8), C(77.4), O(10.8)
Lipid—sphingomyelin	H(11.7), C(68.9), N(3.9), O(11.2), P(4.3)
Mucin	H(4.8), C(34.3), O(60.9)
Protein	H(6.6), C(53.4), N(17.0), O(22.0), S(1.0)
Urea	H(6.7), C(20.0), N(46.7), O(26.6)
Water	H(11.2), O(88.8)

The elemental compositions quoted for carbohydrates, lipids and proteins are the averages of variable biological substances.

TABLE III

THE ELEMENTAL COMPOSITIONS OF THE BODY TISSUES

Body tissue	Elemental composition (% by mass)					Densities		
						Mass	Electron	
	H	C	N	O	Elements with $Z > 8$	kg m^{-3}	el. kg^{-1} $\times 10^{26}$	el. m^{-3} $\times 10^{26}$
Adipose tissue 1	11.2	51.7	1.3	35.5	Na(0.1), S(0.1), Cl(0.1)	970	3.342	3241
Adipose tissue 2	11.4	59.8	0.7	27.8	Na(0.1), S(0.1), Cl(0.1)	950	3.347	3180
Adipose tissue 3	11.6	68.1	0.2	19.8	Na(0.1), S(0.1), Cl(0.1)	930	3.353	3118
Adrenal gland	10.6	28.4	2.6	57.8	P(0.1), S(0.2), Cl(0.2), K(0.1)	1030	3.324	3424
Aorta	9.9	14.7	4.2	69.8	Na(0.2), P(0.4), S(0.3), K(0.1), Ca(0.4)	1050	3.304	3469
Blood—erythrocytes	9.5	19.0	5.9	64.6	P(0.1), S(0.3), Cl(0.2), K(0.3), Fe (0.1)	1090	3.291	3588
Blood—plasma	10.8	4.1	1.1	83.2	Na(0.3), S(0.1), Cl(0.4)	1026	3.330	3417
Blood—whole	10.2	11.0	3.3	74.5	Na(0.1), P(0.1), S(0.2), Cl(0.3), K(0.2), Fe(0.1)	1060	3.312	3511
Brain—cerebrospinal fluid	11.1	—	—	88.0	Na(0.5), Cl(0.4)	1010	3.339	3373
Brain—grey matter	10.7	9.5	1.8	76.7	Na(0.2), P(0.3), S(0.2), Cl(0.3), K(0.3)	1040	3.327	3460
Brain—white matter	10.6	19.4	2.5	66.1	Na(0.2), P(0.4), S(0.2), Cl(0.3), K(0.3)	1040	3.324	3457
Connective tissue	9.4	20.7	6.2	62.2	Na(0.6), S(0.6), Cl(0.3)	1120	3.288	3683
Eye lens	9.6	19.5	5.7	64.6	Na(0.1), P(0.1), S(0.3), Cl(0.1)	1070	3.295	3525
Gallbladder—bile	10.8	6.1	0.1	82.2	Na(0.4), Cl(0.4)	1030	3.330	3430
Gastrointestinal tract—small intestine (wall)	10.6	11.5	2.2	75.1	Na(0.1), P(0.1), S(0.1), Cl(0.2), K(0.1)	1030	3.325	3424
Gastrointenstinal tract—stomach	10.4	13.9	2.9	72.1	Na(0.1), P(0.1), S(0.2), Cl(0.1), K(0.2)	1050	3.319	3485
Heart 1	10.3	17.5	3.1	68.1	Na(0.1), P(0.2), S(0.2), Cl(0.2), K(0.3)	1050	3.315	3481
Heart 2	10.4	13.9	2.9	71.8	Na(0.1), P(0.2), S(0.2), Cl(0.2), K(0.3)	1050	3.318	3484
Heart 3	10.4	10.3	2.7	75.6	Na(0.1), P(0.2), S(0.2), Cl(0.2), K(0.3)	1050	3.318	3484
Heart—blood filled	10.3	12.1	3.2	73.4	Na(0.1), P(0.1), S(0.2), Cl(0.3), K(0.2), Fe(0.1)	1060	3.315	3514
Kidney 1	10.2	16.0	3.4	69.3	Na(0.2), P(0.2), S(0.2), Cl(0.2), K(0.2), Ca(0.1)	1050	3.312	3478
Kidney 2	10.3	13.2	3.0	72.4	Na(0.2), P(0.2), S(0.2), Cl(0.2), K(0.2), Ca(0.1)	1050	3.315	3481
Kidney 3	10.4	10.6	2.7	75.2	Na(0.2), P(0.2), S(0.2), Cl(0.2), K(0.2), Ca(0.1)	1050	3.318	3484
Liver 1	10.3	15.6	2.7	70.1	Na(0.2), P(0.3), S(0.3), Cl(0.2), K(0.3)	1050	3.315	3480
Liver 2	10.2	13.9	3.0	71.6	Na(0.2), P(0.3), S(0.3), Cl(0.2), K(0.3)	1060	3.312	3511
Liver 3	10.1	12.6	3.3	72.7	Na(0.2), P(0.3), S(0.3), Cl(0.2), K(0.3)	1070	3.309	3541
Lung—parenchyma	10.3	10.1	2.9	75.5	Na(0.2), P(0.2), S(0.3), Cl(0.3), K(0.2)	1050	3.315	3481
Lung—blood-filled	10.3	10.5	3.1	74.9	Na(0.2), P(0.2), S(0.3), Cl(0.3), K(0.2)	1050*	3.315	3481

TABLE III—*continued*

Body tissue	Elemental composition (% by mass)					Densities		
						Mass	Electron	
	H	C	N	O	Elements with $Z > 8$	kg m^{-3}	el kg^{-1} $\times 10^{26}$	el. m^{-3} $\times 10^{26}$
Mammary gland 1	10.9	50.6	2.3	35.8	Na(0.1), P(0.1), S(0.1), Cl(0.1)	990	3.333	3299
Mammary gland 2	10.6	33.2	3.0	52.7	Na(0.1), P(0.1), S(0.2), Cl(0.1)	1020	3.324	3391
Mammary gland 3	10.2	15.8	3.7	69.8	Na(0.1), P(0.1), S(0.2), Cl(0.1)	1060	3.313	3512
Muscle—skeletal 1	10.1	17.1	3.6	68.1	Na(0.1), P(0.2), S(0.3), Cl(0.1), K(0.4)	1050	3.309	3475
Muscle—skeletal 2	10.2	14.3	3.4	71.0	Na(0.1), P(0.2), S(0.3), Cl(0.1), K(0.4)	1050	3.312	3478
Muscle—skeletal 3	10.2	11.2	3.0	74.5	Na(0.1), P(0.2), S(0.3), Cl(0.1), K(0.4)	1050	3.312	3478
Ovary	10.5	9.3	2.4	76.8	Na(0.2), P(0.2), S(0.2), Cl(0.2), K(0.2)	1050	3.321	3487
Pancreas	10.6	16.9	2.2	69.4	Na(0.2), P(0.2), S(0.1), Cl(0.2), K(0.2)	1040	3.324	3457
Prostate	10.5	8.9	2.5	77.4	Na(0.2), P(0.1), S(0.2), K(0.2)	1040	3.322	3455
Skeleton—cartilage	9.6	9.9	2.2	74.4	Na(0.5), P(2.2), S(0.9), Cl(0.3)	1100	3.292	3622
Skeleton—cortical bone	3.4	15.5	4.2	43.5	Na(0.1), Mg(0.2), P(10.3), S(0.3), Ca(22.5)	1920	3.100	5952
Skeleton—red marrow	10.5	41.4	3.4	43.9	P(0.1), S(0.2), Cl(0.2), K(0.2), Fe(0.1)	1030	3.321	3420
Skeleton—spongiosa	8.5	40.4	2.8	36.7	Na(0.1), Mg(0.1), P(3.4), S(0.2), Cl(0.2), K(0.1), Ca(7.4), Fe(0.1)	1180	3.258	3844
Skeleton—yellow marrow	11.5	64.4	0.7	23.1	Na(0.1), S(0.1), Cl(0.1)	980	3.350	3283
Skin 1	10.0	25.0	4.6	59.4	Na(0.2), P(0.1), S(0.3), Cl(0.3), K(0.1)	1090	3.306	3604
Skin 2	10.0	20.4	4.2	64.5	Na(0.2), P(0.1), S(0.2), Cl(0.3), K(0.1)	1090	3.306	3604
Skin 3	10.1	15.8	3.7	69.5	Na(0.2), P(0.1), S(0.2), Cl(0.3), K(0.1)	1090	3.309	3607
Spleen	10.3	11.3	3.2	74.1	Na(0.1), P(0.3), S(0.2), Cl(0.2), K(0.3)	1060	3.315	3514
Testis	10.6	9.9	2.0	76.6	Na(0.2), P(0.1), S(0.2), Cl(0.2), K(0.2)	1040	3.324	3457
Thyroid	10.4	11.9	2.4	74.5	Na(0.2), P(0.1), S(0.1), Cl(0.2), K(0.1), I(0.1)	1050	3.318	3484
Trachea	10.1	13.9	3.3	71.3	Na(0.1), P(0.4), S(0.4), Cl(0.1), K(0.4)	1060	3.309	3508
Urinary bladder—urine	11.0	0.5	1.0	86.2	Na(0.4), P(0.1), Cl(0.6), K(0.2)	1020	3.336	3403
Urinary bladder—empty	10.5	9.6	2.6	76.1	Na(0.2), P(0.2), S(0.2), Cl(0.3), K(0.3)	1040	3.321	3454
Urinary bladder—filled	10.8	3.5	1.5	83.0	Na(0.3), P(0.1), S(0.1), Cl(0.5), K(0.2)	1030	3.330	3430

*Mass density of the *inflated* lung is often quoted as 260 kg m^{-3}.

compositions reported by ICRP (1975). As such, the new data remove many of the discrepancies and anomalies present in older studies. Consequently, there may be appreciable differences in C, H, N and O contents compared with previous published data relating to "average" or "typical" body tissues.

For seven tissues (adipose tissue, heart, kidney, liver, mammary gland, muscle—skeletal and skin) sufficient reliable data were available to establish the expected spread in composition. Certain of these, such as adipose tissue (lipid: 61.4–87.3% by mass) and mammary gland (lipid: 5.6–56.2% by mass), exhibited widely varying compositions. On the other hand, the results for liver (water: 72.8–75.6% by mass) were less variable.

The mean composition for muscle—skeletal (No. 2) is very close to that published by ICRU (1964). In that publication the H, C, N and O contents were 10.2%, 12.3%, 3.5% and 72.9% by mass, respectively, compared with 10.2%, 14.3%, 3.4% and 71.0% by mass in this study. This differs from the composition given by ICRP (1975), which appears to include certain protein data from paediatric sources, resulting in a lower nitrogen content.

A major problem with the derivation of mean body tissue compositions is the variability of reported data. This is due to a multitude of reasons: age, sex and state

TABLE IV

THE ELEMENTAL COMPOSITIONS AND MASS DENSITIES OF ADULT AND CHILD CORTICAL BONE (WOODARD, 1986)

Sample	Elemental composition (% by mass)					Mass density kg m^{-3}
	H	C	N	O	Others	
24 adults (20–74 years)	3.4	15.5	4.2	43.5	0.1 Na, 0.2 Mg, 10.3 P, 0.3 S, 22.5 Ca	1920
10 children (6–13 years)	3.9	15.8	4.4	45.0	0.2 Mg, 9.8 P, 20.9 Ca	1830
4 children (2–5 years)	4.0	15.7	4.5	45.4	0.2 Mg, 10.1 P, 20.1 Ca	1800
Perinatal rhesus monkey	6.7	15.2	4.9	56.7	0.1 Mg, 5.0 P, 11.4 Ca	1400

of health of the subject and the differing experimental procedures adopted for the analyses. The variation with age is demonstrated in Table IV, which includes previously unpublished data on the cortical bones of paediatric subjects measured by one of the authors (H.Q.W.). The wetter, younger bones are seen to have less calcium and lower mass densities than the adult counterparts.

More comprehensive measurements on the compositions of healthy adult body tissues are urgently needed. Recent studies have tended to concentrate on trace-elements, ignoring the important elements H, C, N and O, which make up some 99% by mass of soft tissues. The high-atomic-number elements, Na, P, S, Cl, K and Ca, are important at low and high photon energies in both soft and skeletal tissues and their presence may affect radiation dosimetry (Laughlin et al, 1987). In particular, adipose tissue (subcutaneous deposits, intra-abdominal and yellow marrow), gastrointestinal tract-intestine (small and large), liver, muscle—skeletal, skeleton—cartilage, skeleton—red marrow and urinary bladder wall need more investigation Similar measurements are also required for diseased and paediatric body tissues.

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REFERENCES

Albritton, E C., 1952 *Standard Values in Blood* (W. B. Saunders, Philadelphia; American Institute of Biological Sciences and the National Research Council), p. 5.

Altman, P L & Dittmer, D S., 1961. *Blood and Other Body Fluids* (Federation of American Societies for Experimental Biology, Washington).

Baker, G L, 1969 Human adipose tissue composition and age *American Journal of Clinical Nutrition, 22,* 829–835.

Block, E, 1951. Quantitative morphological investigations of the follicular system in women. methods of quantitative determinations *Acta Anatomica, 12,* 267–285

Brincat, M., Moniz, C F., Studd, J W. W, Darby, A. J, Magos, A & Cooper, D, 1983 Sex hormones and skin collagen content in postmenopausal women *British Medical Journal, 287,* 1337–1338

Cander, L. & Forster, R. E., 1959 Determination of pulmonary parenchymal tissue volume and pulmonary capillary blood flow in man *Journal of Applied Physiology, 14,* 541–545

Diem, K., 1962 *Documenta Geigy Scientific Tables,* 6th edit. (Geigy Pharmaceuticals, Ardsley, New York)

Dittmer, D S & Grebe, R. M., 1959. *Handbook of Circulation* (W. B Saunders, Philadelphia)

Dju, M. Y, Mason, K. E. & Filer, L J, Jr, 1958 Vitamin E (tocopherol) in human tissues from birth to old age. *American Journal of Clinical Nutrition, 6,* 50–60.

Eisenstein, A B., 1967 Nutritional factors and the adrenal cortex. In *The Adrenal Cortex.* Ed by A. B Eisenstein (Little, Brown & Co., Boston), p. 330

Entenman, C., Goldwater, W. H, Ayres, N. S. & Behnke, A. R., Jr, 1958. Analysis of adipose tissue in relation to body weight loss in man *Journal of Applied Physiology, 13,* 129–134.

Eve, I S., 1966 A review of the physiology of the gastrointestinal tract in relation to radiation doses from radioactive materials. *Health Physics, 12,* 131–161.

Fieser, L. F. & Fieser, M., 1963 *Advanced Organic Chemistry.* (Reinhold, New York), pp 1007–1008.

Fillerup, D. L. & Mead, J. F., 1967. The lipids of the ageing human brain. *Lipids, 2,* 295–298.

Fomon, S J., 1966. Body composition of the infant. I. The male "reference infant". In *Human Development* Ed. by F. Falkner (W. B Saunders, Philadelphia, London), pp. 239–245.

Forbes, R M, Cooper, A. R. & Mitchell, H. H., 1953. The composition of the adult human body as determined by chemical analysis. *Journal of Biological Chemistry, 203,* 359–366

Forbes, R M., Mitchell, H. H & Cooper, A R., 1956. Further studies on the gross composition and mineral elements of the adult human body. *Journal of Biological Chemistry, 223,* 969–975.

Fowler, J. F. & Young, A. E., 1959. The average density of healthy lung. *American Journal of Roentgenology, 81,* 312–315

Friedman, C. E, 1951 Heart volume, myocardial volume and total capacity of the heart cavities in certain chronic heart diseases. *Acta Medica Scandinavica and Supplements, 257,* 1–100.

Goldberg, D M., Goudie, R B & Ayre, H. A., 1968. Effect of disease on chemical constituents of the human thyroid gland *Journal of Clinical Endocrinological Metabolism, 28,* 41–48

Hammerstein, G. R, Miller, D. W., White, D R, Masterson, M E, Woodard, H. Q & Laughlin, J. S., 1979 Absorbed radiation dose in mammography. *Radiology, 130,* 485–491.

Handbook of Chemistry and Physics, 1982 62nd edit (CRC Press, Inc., Boca Raton, Florida)

Hildes, J. A, Sherlock, S & Walshe, V., 1949 Liver and muscle glycogen in normal subjects, in diabetes mellitus and in acute hepatitis: Part I. Under basal conditions. *Clinical Science, 7,* 287–295.

Himwich, W A. & Himwich, H E, 1957. Brain composition during the whole life span. *Geriatrics, 12,* 19–27

Houssay, B. A, Lewis, J T, Orías, O., Braun, E., Menéndez, Hug, E, Foglia, V G. & Leloir, L. F, 1955 *Human Physiology,* 2nd edit (McGraw-Hill, New York).

ICRU, 1964 *Physical Aspects of Irradiation.* ICRU Report 10b, published as NBS Handbook 85 (ICRU, Bethesda, Maryland)

——1975 *Report on the Task Group on Reference Man* ICRP Report 23 (Pergamon, Oxford).

——1977 *Neutron Dosimetry for Biology and Medicine* ICRU Report 26 (ICRU, Bethesda, Maryland).

Ikawa, M, Impraim, C C., Wang, G. & Yoshida, A., 1983. Isolation and characterisation of aldehyde dehydrogenase isozymes from usual and atypical human livers. *Journal of Biological Chemistry, 258,* 6282–6287.

Jorulf, H, 1975 Roentgen diagnosis of intraperitoneal fluid—a physical, anatomic and clinical investigation. Ph.D. Thesis, University of Uppsala.

Kerr, G D', 1982. Photon and neutron fluence-to-kerma conversion factors for ICRP-1975 Reference Man using improved elemental compositions for bone and marrow of the skeleton *Oak Ridge National Laboratory Report*, ORNL/TM-8318 (Oak Ridge, Tennessee).

KEYS, A. & BROŽEK, J., 1953 Body fat in adult man *Physiological Reviews, 33*, 245–325.

KIRK, J. E., 1962. Arterial and arteriolar systems: G. biochemistry. In *Blood Vessels and Lymphatics* Ed. by D. I Abramson (Academic Press, New York, London), pp 211–217

LAUGHLIN, J. S., MOHAN, R. & KUTCHER, G J, 1987 Choice of optimum megavoltage for accelerators for photon beam treatment. Proceedings of 3rd Annual Meeting of ESTRO, Jerusalem, Israel *International Journal of Radiation Oncology, Biology and Physics*, in press

LONG, C., KING, E. J. & SPERRY, W. M., 1961. *Biochemist's Handbook* (D. van Nostrand, Princeton).

MCILWAIN, H, 1959. *Biochemistry and the Central Nervous System*, 2nd edit. (Little, Brown & Co., Boston)

MARTINSSON, A., 1967 On the composition of human adipose tissue *Acta Medica Scandinavica, 182*, 795–803.

MITCHELL, H. H., HAMILTON, T. S., STEGGERDA, F. R. & BEAN, H. W., 1945. The chemical composition of the adult human body and its bearing on the biochemistry of growth. *Journal of Biological Chemistry, 158*, 625–637

MORSE, W I. & SOELDNER, J. S., 1963. The composition of adipose tissue and the nonadipose body of obese and nonobese man *Metabolism, 12*, 99–107

——1965. The measurement of human adipose tissue mass. In *Handbook of Physiology, Adipose Tissue*. Ed. by A E. Renold and G F Cahill Jr (American Physiological Society, Washington).

NEUFELD, A. H., 1937. Contributions to the biochemistry of bromine. II. The bromine content of human tissues *Canadian Journal of Research, 15B*, 132–138.

OSER, B L., 1965 *Hawk's Physiological Chemistry*, 14th edit (McGraw-Hill, New York)

PAWAN, G L. S & CLODE, M., 1960. The gross chemical composition of subcutaneous adipose tissue in the lean and obese human subject. *Biochemical Journal, 74*, 9P

ROTHMAN, S, 1954. *Physiology and Biochemistry of the Skin* (University of Chicago Press, Chicago).

SAUNDERS, D. R., WAYS, P. O, PARMENTIER, C M. & RUBIN, C. E., 1966. Studies on the lipid composition of human small bowel mucosa. *Journal of Clinical Investigation, 45*, 1516–1525.

SCAMMON, R. E. & HESDORFFER, M. B., 1937 Growth in mass and volume of the human lens in postnatal life *Archives of Ophthalmology, 17*, 104–112.

SHOHL, A. T., 1939 *Mineral Metabolism* (Reinhold Publishing Corporation, New York)

SLATER, T. F, SAWYER, B. & STRÄULI, U, 1964 Deoxyribonucleic acid and ribonucleic acid content of human tissues obtained at necropsy *Journal of Clinical Pathology, 17*, 554–556

SPECTOR, W. S., 1956. *Handbook of Biological Data* (W B. Saunders, Philadelphia)

TANDON, G K., PANT, M. C., NEGI, V K. & MEHROTRA, H. N., 1978. Changes in serum proteins, non-protein nitrogen and urea content in ergometric exercise—a preliminary communication *Indian Journal of Medical Research, 67*, 329–331

THOMAS, L. W, 1962 The chemical composition of adipose tissue of man and mice. *Quarterly Journal of Experimental Physiology, 47*, 179–188

TIPTON, I. H. & COOK, M. J, 1963. Trace elements in human tissue: II. Adult subjects from the United States. *Health Physics, 9*, 103–145.

WHITE, D. R. & FITZGERALD, M., 1977. Calculated attenuation and energy absorption coefficients for ICRP Reference Man (1975) organs and tissues. *Health Physics, 33*, 73–81.

WIDDOWSON, E. M. & DICKERSON, J W T, 1960. The effect of growth and function on the chemical composition of soft tissues. *Biochemical Journal, 77*, 30–43

——1964. Chemical composition of the body. In *Mineral Metabolism*. Ed by C. L. Comar & F. Bronner (Academic Press, New York), Vol. 2, pp. 1–247

WIDDOWSON, E. M., MCCANCE, R A. & SPRAY, C. M, 1951. The chemical composition of the human body *Clinical Science, 10*, 113–125.

WINTROBE, M. M., 1967. *Clinical Haematology*, 6th edit (Lea & Febiger, Philadelphia).

WOODARD, H. Q., 1986. Unpublished data.

WOODARD, H. Q. & WHITE, D R, 1982 Bone models for use in radiotherapy dosimetry *British Journal of Radiology, 55*, 277–282.

WOOTTON, I. D. P. & FREEMAN, H, 1982 *Microanalysis in Medical Biochemistry*, 6th edit (Churchill Livingstone, Edinburgh).

1986, *The British Journal of Radiology*, 59, 1219–1223 DECEMBER 1986

Technical notes

Rotational panoramic radiography: a comparison of radiation doses in the standard and reverse positions

By F. J. Williams, M.Sc., F. R. Hudson, F.Inst. P. and *A. F. Markus, F.D.S.R.C.S.

Physics Department and *Department of Oral Surgery, Mount Vernon Hospital, Northwood, Middlesex

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Rotational panoramic radiography is now well established as a valuable technique in the diagnosis of oral and facial disorders. The theory of the technique was originally described by Numata (1933, 1934) and subsequently by Paatero (1946, 1954, 1961). Analyses of the radiation doses have been reported widely (*e.g.* Casebow, 1973; Nyström et al, 1975; Wall et al, 1979; Bartolotta et al, 1983). The dosage received is considerably lower than that for an equivalent survey of the dental structures with conventional intra-oral radiographic techniques (Wall et al, 1979).

One disadvantage associated with the technique, however, is that the image quality does not permit the resolution of all the structures which may be of importance in the assessment of patient status. A number of variations on the basic technique have been proposed in the literature by workers seeking to improve the quality of the radiographs in particular situations, *e.g.* Greig and Musaph (1973). Markus et al (1986) have demonstrated that significant improvement in the visualisation of the temporomandibular joint (TMJ) and associated structures is possible if the patient is placed in the reverse position (Fig. 1). Obvious questions arise as to the effect of the repositioning on the doses received by sensitive structures, particularly the lens of the eye.

We have carried out a series of measurements to investigate the effect of patient position on radiation dose distributions.

MATERIALS AND METHODS

The study was carried out using a Siemens Orthopantomograph OP3S set operated under the standard conditions used in the department (70 kV, 225 mAs). The X-ray tube and the film cassette both rotate about an axis through the position of the oral cavity. The film cassette rotates simultaneously on its own axis, such that at any instant one sector of the jaw only is in sharp focus on the film. The rotation pattern is illustrated in Fig. 1.

Measurements were first made with X-ray film (Agfa Gevaert 15 cm × 30 cm Dentus RP5 PE/KW) mounted on a series of phantoms to permit a simple visualisation

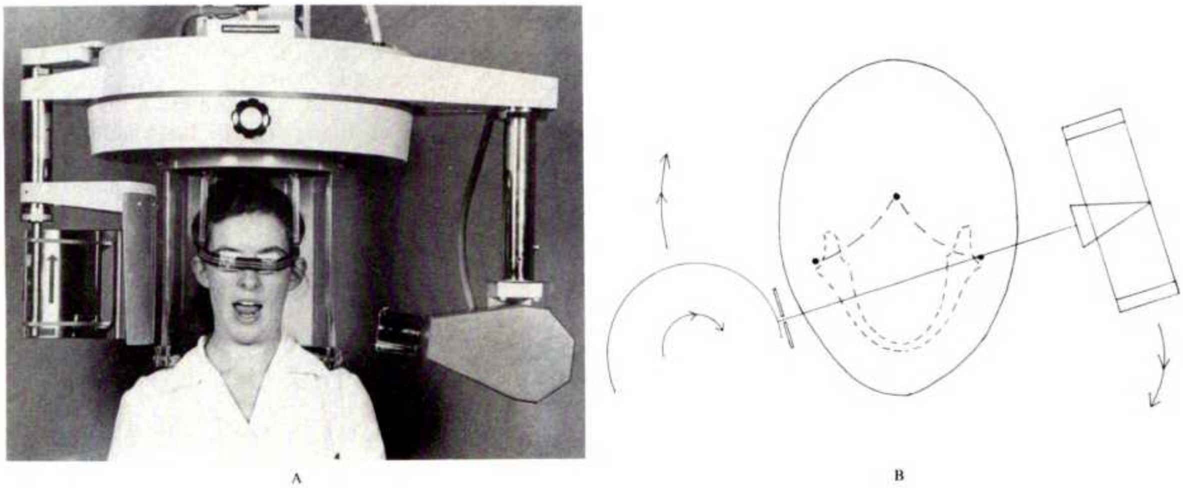

FIG. 1.

(A) Position of head in relation to X-ray tube and film holder for reverse position orthopantomography. (B) Geometry used in the exposure.

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*Present address: Department of Oral and Maxillo Facial Surgery, Poole General Hospital, Poole, Dorset.

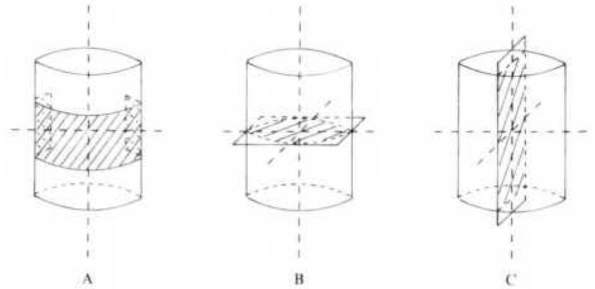

FIG. 2.

Positions used for mounting films on the three phantoms used. (A) Surface dose phantom, (B) Rando phantom, (C) sagittal phantom.

of the dose distributions. The first phantom used was a thin-walled plastic cylinder, of diameter 165 mm, filled with water. The diameter was a simple but appropriate compromise to the varying sections of the adult skull. The second phantom used was the Rando head and neck section (Alderson Research Laboratories). This phantom, made of tissue-equivalent synthetic rubber, contains a complete human skull with all bony structures and airways. The last phantom, prepared from wax, approximated head and neck dimensions, but was sectioned sagittally through the central plane.

The positions used to mount films in the three phantoms are shown schematically in Fig. 2. The spatial-distribution data gained from the films was supplemented by measurements from thermoluminescent dosemeters (3 mm × 3 mm × 0.9 mm lithium fluoride chips (TLD 100)). These were exposed under comparable conditions to those used for the film exposures, except that multiple exposures (× 10) were used to increase reading accuracy. The chips were standardised against the dose delivered by a calibrated radiotherapy treatment machine operated at 75 kV.

RESULTS

The track of the X-ray field on a film mounted on the surface of the water phantom demonstrated the form of the surface dose observed for a standard position exposure (Fig. 3). It can be seen that there is a relatively sharp upper and lower border and that the effect of the three centres of rotation is to produce higher exposures at the extremities of the track. At an energy of 70 kV it is clear that the major contribution to the surface dose will come from the direct incident rather than the transmitted radiation.

Comparison of scans of the films for the standard and reverse positions shows that there is no significant change in the surface area of the phantom exposed to the beam, although the maximum dose is higher when the reverse position is used. In both the standard and reverse positions, the level of the eyes, with correct alignment, will lie outside the borders of the high-dose region of the X-ray field.

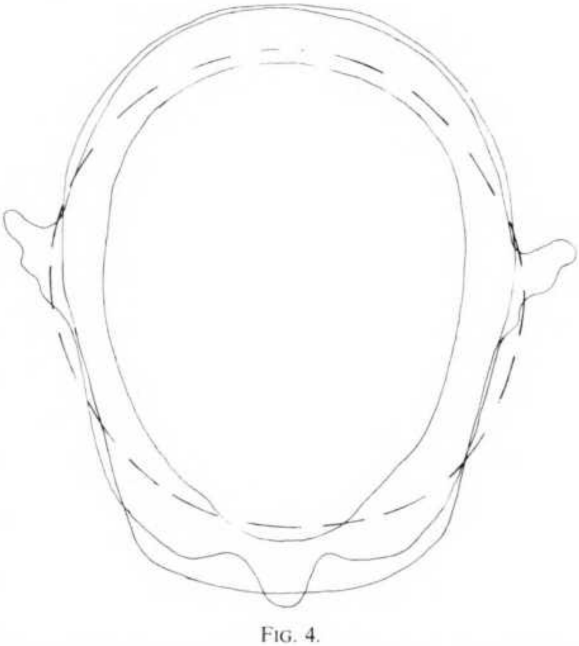

FIG. 4.

Superposition of three 25 mm-thick sections of the Rando phantom on a circle 165 mm in diameter.

By superimposing three 2.5 cm-thick sections of the Rando phantom on the section of the phantom used (Fig. 4), the deviation of the Rando section from the cylindrical phantom is calculated to range from −22 mm to +22 mm. For an X-ray set operated at

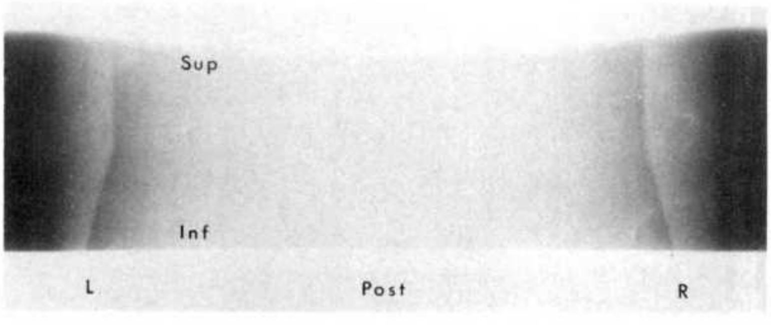

FIG. 3.

Track of X-ray field on the surface of the cylindrical phantom (diameter 165 mm) for a standard orthopantomogram.

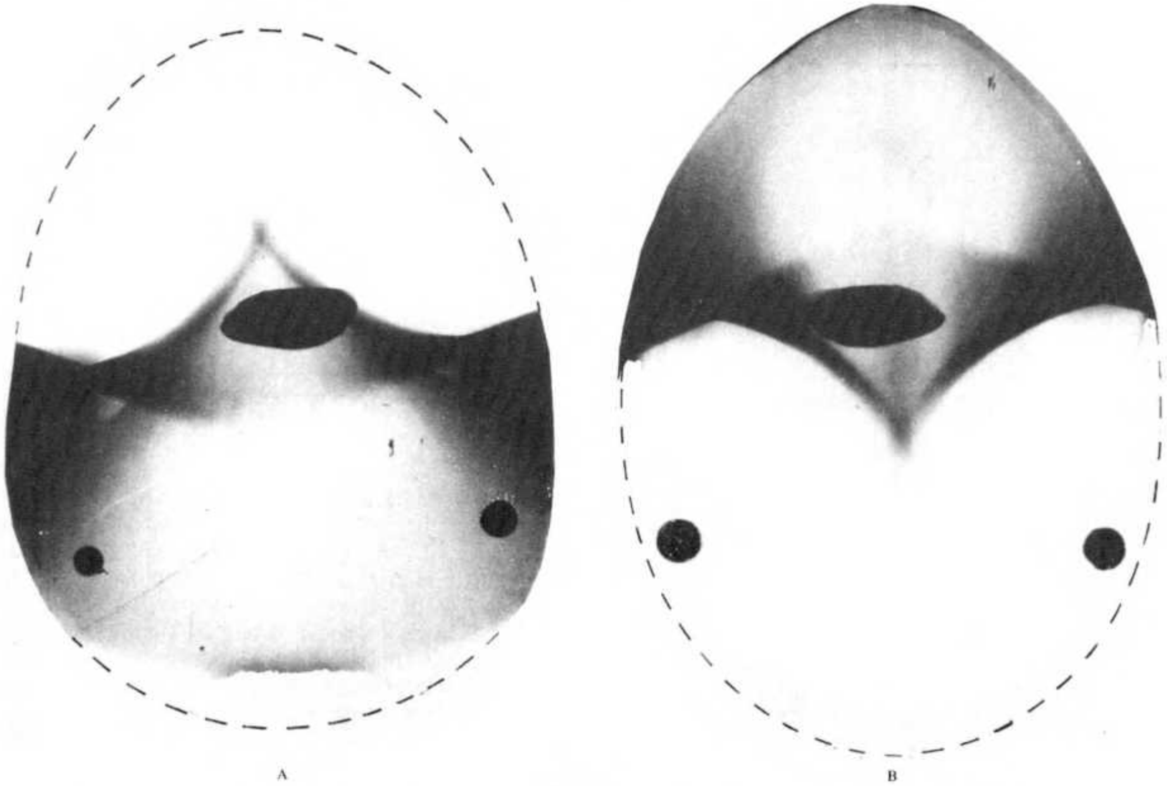

FIG. 5.

Complex dose distribution observed on radiographs exposed in the Rando phantom during (A) standard and (B) reverse orthopantomography. Clearly visible is the oropharynx and the sites of the two fixing pegs of the phantom.

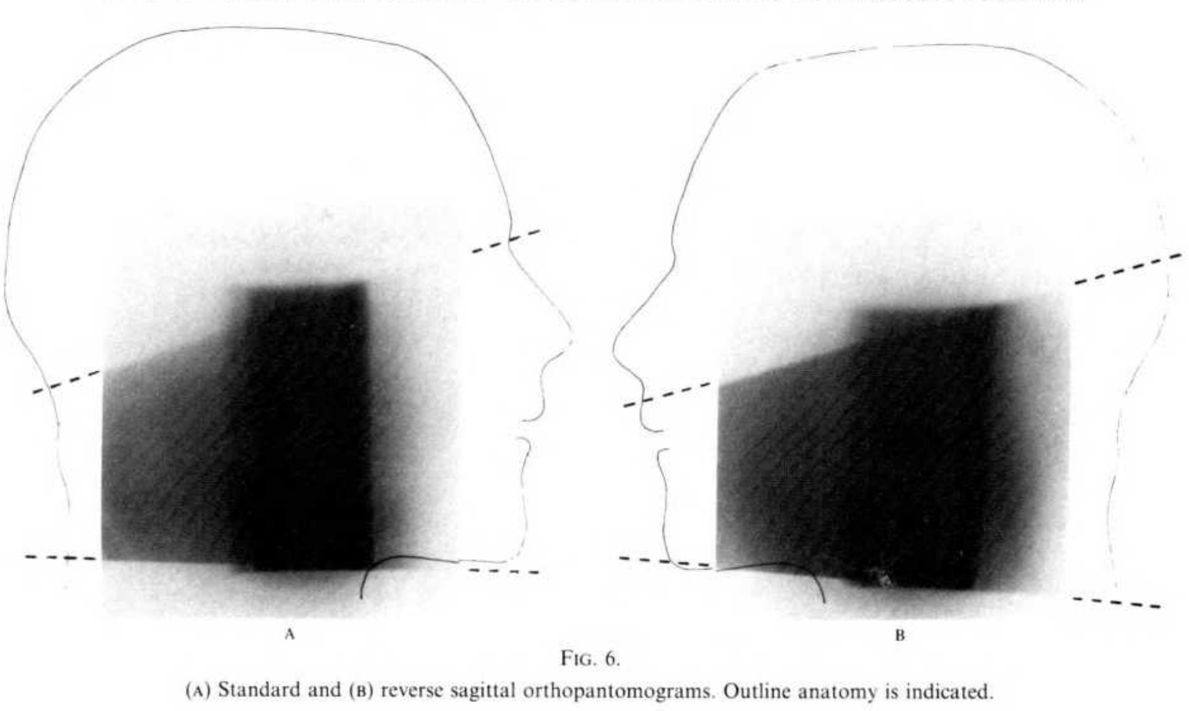

FIG. 6.

(A) Standard and (B) reverse sagittal orthopantomograms. Outline anatomy is indicated.

TABLE I

DOSES TO SELECTED SITES OF RANDO PHANTOM

Sites	This work		Bartolotta et al (1983) (standard, cGy)	Wall et al (1979) (standard, cGy)
	Standard (cGy)	Reverse (cGy)		
Left eye	0.002	0.003	0.002	0.002
Right eye	0.002	0.003		
Left external TMJ	0.007	0 010		
Right external TMJ	0.006	0 007		
Left mastoid	0 006	0.006		
Right mastoid	0.005	0.004		
Back neck	0.008	0.002	0.100	0.12
Centre tongue	0.013*	0.035*	0.024†	0 22†

*Position 2 cm posterior to skin surface midline, but at a level 1 cm above point of contact between upper and lower lips.
†Position not specified.

20 cm focus–skin distance, these deviations would correspond to changes in field size of ±10% and to changes in dose of ±20%.

Radiographs taken with the Rando phantom through the level of the upper teeth (Fig. 5) clearly demonstrate the complex exposure pattern which can be related to that seen in the other radiographs. Thus the area of high dose visible at the end of the track in Fig. 3 can be seen to match the skin surface over the lateral foci of the rotation. It can be seen that there is little difference in the absolute radiation distribution between the standard and reverse positions

Radiographs taken with the phantom made from wax show the exposure pattern in the central sagittal section of the phantom (Fig. 6). These radiographs clearly show the well defined upper and lower border of the field and also reveal the inhomogeneity of the dose distribution caused by the triple-focus motion of the set. Scans of these films show a dose gradient of some 30% from the inferior to the superior border, but the structure of the distribution remains constant. The gradient reflects the vertical angulation of the beams.

The sagittal radiographs make patent the preservation of the shape of the dose distribution through the full height of the exposed volume. They also show that the triple-focus density distribution is essentially reversed in relation to the anatomy in the reverse position, and consequently the mean energy imparted to the patient will not change significantly.

The doses assigned to selected sites in the exposure of the Rando phantom in the standard and reverse positions as measured using TLDs are listed in Table I.

While detailed comparison with the results of other workers is complicated by the inhomogeneous nature of the X-ray field, it is clear that no unacceptable change in dose level is observed when the reverse position is used. In particular, the estimated dose to the lens remains low.

DISCUSSION

Radiographic measurements have been made to determine the effect on the dose distribution in the patient in orthopantomography when the reverse position of Markus et al (1986) is used to improve definition of the TMJ. The radiographs clearly show the complexity of the dose distribution, but the sagittal radiographs in particular make evident the degree of constancy of the distribution in the vertical direction. The TLD measurements taken in similar geometry show no unacceptable changes in organ exposure. It is concluded that no unexpected hazard should be met from a correctly set-up reverse position tomogram.

However, the rapid variation in dose distributions observed within the field confirms that interpretation of isolated TLD measurements alone has major limitations. Comparison of exposures from different techniques should use methods that enable the irradiated volume to be delineated. Extending this to provide a measure of the mean energy imparted should be the final objective. Nyström et al (1975) have compared their estimate of 450 g rad per study with van Aken and van der Linden's (1966) estimate of 109 g rad and have concluded that these results are not incompatible. Clearly, further development in techniques is called for.

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REFERENCES

BARTOLOTTA, A., CALENDA, E., CALICCHIA, A. & INDOVINA, P. L., 1983 Dental orthopantomography survey of patient dose. *Radiology, 146*, 821–823

CASEBOW, M. P., 1973. Patient doses from orthopantomograph dental X-ray exposures. *British Journal of Radiology, 46*, 230–232

GREIG, J. H. & MUSAPH, F. W., 1973. A method of radiological demonstration of the temporomandibular joints using the orthopantomograph *Radiology, 106*, 307–310

MARKUS, A. F., POSWILLO, D. E. & SEMPLE, J, 1986 The reverse orthopantomogram *British Dental Journal*, in press

NUMATA, H., 1933. Consideration of the parabolic radiography of the dental arch *Journal of Shimizu Studies, 10*, 13 (Japanese).

NUMATA, H., 1934. A trial on the narrow beam radiography *Journal of Shimizu Studies*, *12*, 6 (Japanese).

NYSTRÖM, O., WELANDER, U. & WICKMAN, G., 1975. The distribution of absorbed dose and mean energy imparted in orthopantomography. *Dentomaxillofacial Radiology*, *4*, 38–42.

PAATERO, Y. V., 1946. A new radiographic method in dentistry. *Suomen Hammaslääkäriseuran Toimituksia*, *87*, 37–38 (Finnish).

——1954. Pantomography in theory and use. *Acta Radiologica*, *41*, 321–335.

——1961. Pantomography and orthopantomography. *Oral Surgery, Oral Medicine and Oral Pathology*, *14*, 947–953.

VAN AKEN, J. & VAN DER LINDEN, L. W. J., 1966. The integral absorbed dose in conventional and panoramic complete-mouth examinations. *Oral Surgery, Oral Medicine and Oral Pathology*, *22*, 603–616.

WALL, B. F., FISHER, E. S., PAYNTER, R., HUDSON, A. & BIRD, P. D., 1979. Doses to patients from pantomographic and conventional dental radiography. *British Journal of Radiology*, *52*, 727–734.

An autoclavable transport container for guide-wires containing iridium 192

By T. Deans and M. W. Rafferty, M.Sc.

Biophysics Department, Sir Charles Gairdner Hospital, Nedlands, Western Australia 6009

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The use of radioactive ^{192}Ir wire in the treatment of high bile-duct carcinoma has been described by Fletcher et al (1981). At Sir Charles Gairdner Hospital the routine procedure involves initial placement of a nasobiliary catheter into the patient for both biliary drainage and accommodation of a flexible guide-wire containing the prescribed length of ^{192}Ir wire. The guide-wire used is 1450 mm long and contains an inner stilette which is removed to allow a nylon spacer (normally 20 mm in length) followed by the 0.3 mm diameter ^{192}Ir wire (typically 30–100 mm in length) to be inserted into the guide-wire. The stilette is then replaced to locate the spacer and ^{192}Ir wire positively, at the distal end of the guide-wire. The loaded guide-wire is positioned under radiological control and left in the patient until the prescribed treatment dose has been delivered. Before use, the guide-wire containing the ^{192}Ir wire must be autoclaved. A device to permit this and afford radiation protection for staff has been constructed, and is described below.

CONSTRUCTION

The main body of the autoclavable transport container is a stainless-steel tube 50 mm in diameter and 200 mm in length with a mounting plate for the winding mechanism welded at one end. The main body is filled with lead, except for a 4 mm stainless-steel tube mounted coaxially, which extends as far as the outer ring of the winding mechanism. The winding mechanism consists of three main parts.

The outer ring

This is constructed from a linen-based epoxy-resin-filled material known by the trade name "Tufnol". This material was chosen because of its light weight, corrosion resistance and for its ability to withstand repeated autoclaving with minimum distortion. It is attached to the mounting plate of the main body by two screws, as illustrated in Fig. 1.

The inner rotating drum

Also made from Tufnol, this drum has a spring-loaded clip in it to secure the inactive end of the combined guide-wire and stilette. Adjacent to the spring-loaded clip is a machined annular groove which accommodates the guide-wire as it is retracted through the main body of the container.

The securing disc

This stainless-steel disc holds the inner rotating drum within the outer ring. It has a section removed to allow access to the spring-loaded clip which secures the inactive end of the guide-wire to the inner drum. It also has five equally spaced holes drilled through it to facilitate another spring-loaded clip being mounted on the outer ring. This clip locks the position of the inner drum and prevents the active end of a loaded guide-wire from being dislodged from the main body section. On the face of the disc is engraved "Advance" and "Retract" to indicate directions of travel of the guide-wire.

LOADING

The inactive end of the guide-wire is passed through the lead-filled main body to the spring-loaded clip in the inner rotating drum. The guide-wire is then wound into the annular groove until the active ^{192}Ir wire tip is retracted within the lead shielding of the main body. The inner drum is then locked into position to secure the position of the guide-wire. Finally, a stainless-steel

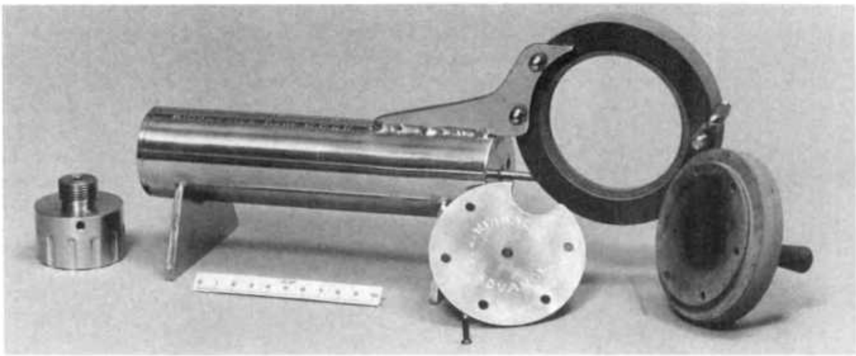

Fig. 1.
Container dismantled for cleaning.

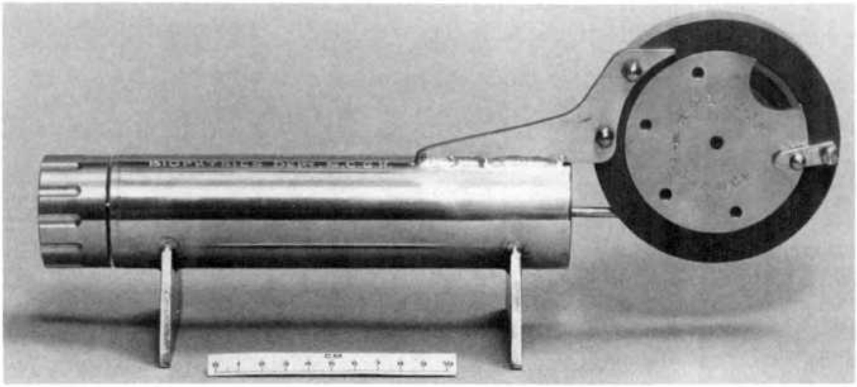

Fig. 2.
Container assembled and ready for autoclaving.

cap, 30 mm long, with a breather hole at 90° to the bore of the main body to allow for the passage of steam during autoclaving, is screwed into position. Figure 2 shows the container loaded with a guide-wire ready for autoclaving.

The device has proven very successful in the preparation of long guide-wires containing ^{192}Ir. The main body provides shielding of four half-value thicknesses for ^{192}Ir γ rays and the total weight of the container is 5 kg. It is simple to load and use, is autoclavable and provides adequate radiation protection for personnel.

Acknowledgments

To Dr B. H. Laurence of the Gastroenterology/Liver Unit who conducts the treatments at this hospital and to Mr P. Klemp of the Medical Physics Department, Royal Perth Hospital, who initially prepares the guide-wires with the prescribed length of ^{192}Ir wire.

REFERENCE

Fletcher, M. S., Brinkley, D., Nunnerley, H., Dawson, J. L., Wheeler, P. G. & Williams, R., 1981. Treatment of high bile duct carcinoma by internal radiotherapy with iridium-192 wire. *Lancet, ii,* 172–174.

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Case reports

Unilateral obstruction of septate uterus: computed tomography and ultrasound appearances

By L. A. Petrich, M.D. and David A. Cory, M.D.

Department of Radiology, Indiana University School of Medicine, 1100 West Michigan St, Indianapolis, IN 46223, USA

(*Received February 1986*)

The characteristic appearances of the fluid-filled uterus on computed tomography (CT) have been well described (Scott et al, 1981). In addition, the use of ultrasound in the diagnosis and elucidation of congenital anomalies of the female genital tract has been reported previously and classification systems have been proposed (Malini et al, 1984). Sonographic detection of such anomalies has been particularly successful during pregnancy and in neonates (Wilson et al, 1978; McArdle & Berezin, 1980). Experience with paediatric and adolescent patients has been less extensive (Haller et al, 1977). We present a case report of an adolescent girl with septate uterus and unilateral obstruction and its appearance on CT and ultrasound.

CASE REPORT

A 13-year-old girl was referred with a 6-month history of daily, sharp, right lower-quadrant pain. Menarche had occurred approximately 4 months before symptoms and menstrual periods were irregular. There were no associated gastrointestinal or urinary complaints. Physical examination was negative, with no masses.

The patient had been investigated in hospital twice before for the same complaints, at the onset of symptoms and again approximately 5 months later. Laboratory data and radiographs were not of diagnostic value. A pelvic ultrasound examination at first admission was interpreted as normal. Laparoscopy during the second admission was reported as normal except for possible endometriosis. She was placed on oral contraceptives without improvement in symptoms.

The patient was referred to this hospital with persistent pain. Oral contraceptives were discontinued and her pain increased. Pelvic ultrasound revealed a 3 cm hypoechoic uterine mass (Fig. 1). Fluid in the cul-de-sac was also seen. Abdominal and pelvic CT scans showed a round, low-density mass in the right side of the uterus (Fig. 2). Both kidneys were normal. On pelvic examination by a gynaecologist, there was a single cervix, but the uterus was tense and one and a half times normal size.

The patient was referred for surgery with a pre-operative diagnosis of septate uterus with obstructed right horn. The septum could not be resected by a combined hysteroscopic/laparoscopic approach. At open operation the diagnosis was confirmed (Fig. 3). The adnexae were normal and there was no evidence of endometriosis. The post-operative course was uneventful and she was discharged on the third post-operative day.

DISCUSSION

In female embryological development, paired Mullerian ducts fuse in the midline to form the uterus, cervix and proximal vagina. Failure of fusion in varying degrees results in congenital anomalies including double uterus (uterus didelphys), bicornuate uterus and septate uterus. As part of the anomalous development, a segment of the uterus may be obstructed. After menarche, as blood accumulates in the obstructed segment, distension of the uterus may result in pain.

Ultrasound and CT play an important role in diagnosis. Pelvic examination performed by anyone unaccustomed to paediatric patients may be falsely

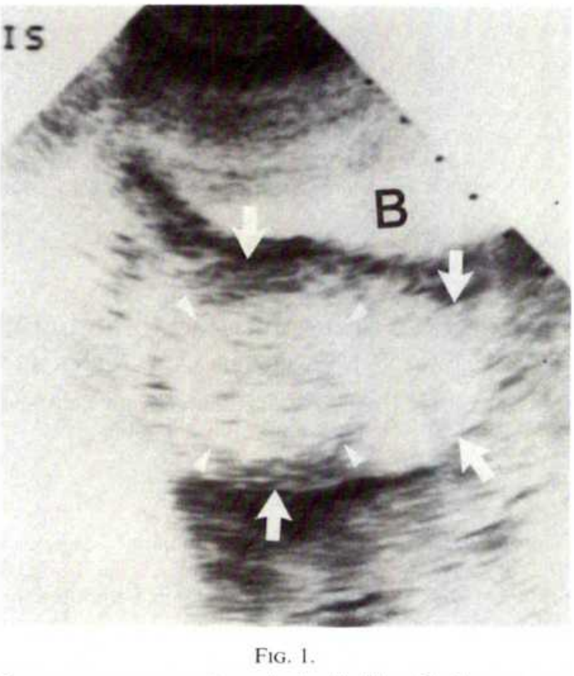

FIG. 1.

Transverse sonogram through the bladder (B) shows uterus (arrows) and smooth, round mass with low-level echoes (arrowheads).

Author for correspondence: Dr D. A. Cory, Department of Radiology, Riley Hospital for Children, 702 Barnhill Drive, Indianapolis, IN 46223, USA.

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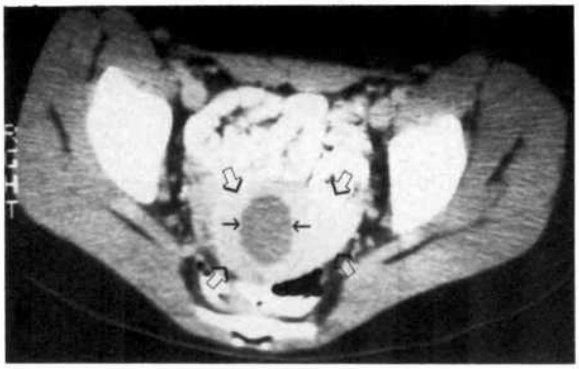

FIG. 2.

Computed tomogram of the pelvis following intravenous, oral, and rectal contrast-medium administration shows a homogeneous, fluid-density mass (black arrows) in the right side of the uterus (open arrows).

negative, especially if the cervix is not duplicated. The abnormality may be overlooked at laparoscopy if the external contour of the uterus is relatively normal, as in septate uterus.

The findings of a rounded, eccentric mass which is of low density on CT, or with uniform low-level echoes on sonography, should lead to the correct diagnosis (Azouz & Williams, 1982; Stangl et al, 1983). Fluid in the cul-de-sac is supporting evidence of obstruction with peritoneal spill via the fallopian tubes.

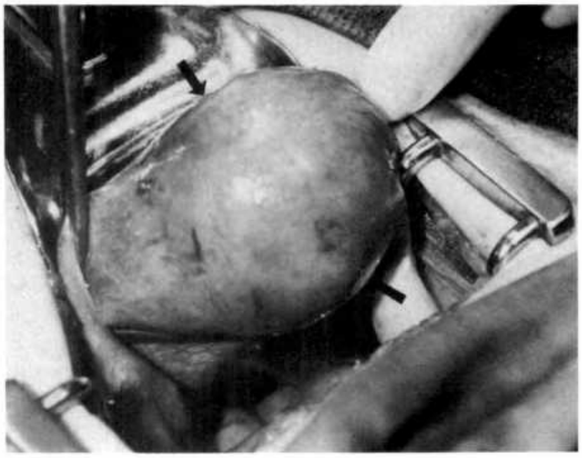

FIG. 3.

At laparotomy the uterus, viewed from above, is enlarged on the right (arrows).

REFERENCES

AZOUZ, E. M. & WILLIAMS, R. L., 1982. Uterus didelphys with unilateral hematometrocolpos and hematosalpinx. *Journal of Computer Assisted Tomography*, *6*, 1028–1031.

HALLER, J. O., SCHNEIDER, M. & KASSNER, E. G., STAIANO, S. J., NOYES, M. B., CAMPOS, E. M. & MCPHERSON, H., 1977. Ultrasonography in pediatric gynecology and obstetrics. *American Journal of Roentgenology*, *128*, 423–429.

MALINI, S., VALDES, C. & MALINAK, L. R., 1984. Sonographic diagnosis and classification of anomalies of the female genital tract. *Journal of Ultrasound in Medicine*, *3*, 397–404.

MCARDLE, C. R. & BEREZIN, A. F., 1980. Ultrasound demonstration of uterus subseptus. *Journal of Clinical Ultrasound*, *8*, 139–141.

SCOTT, W. W., ROSENSHEIN, N. B., SIEGELMAN, S. S. & SANDERS, R. C., 1981. The obstructed uterus. *Radiology*, *141*, 767–770.

STANGL, W., FRANK, R. C., FRANK, W. & NELLI, S., 1983. Sonographic findings in a case of uterine and vaginal duplication (didelphys) with unilateral hematocolpometrasalpinx. *Journal of Clinical Ultrasound*, *11*, 40–41.

WILSON, D. A., STACY, T. M. & SMITH, E. I., 1978. Ultrasound diagnosis of hydrocolpos and hydrometrocolpos. *Radiology*, *128*, 451–454.

Sonographic and computed tomographic findings in Canavan's disease

By P. J. Patel, T. M. Kolawole, A. H. Mahdi and E. A. Wright

Departments of Radiology, Paediatrics, and Pathology, King Khalid University Hospital,
King Saud University, Riyadh, Saudi Arabia

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A proven case of Canavan's disease (spongy degeneration of Van Bogaert-Bertrand type) of the brain is presented with sonography and computed tomography (CT) scans and histological findings. This is, to our knowledge, the first reported case of the sonographic features of Canavan's disease of the brain. This very rare condition can sonographically mimic a number of brain cystic leucomalacias.

CASE REPORT

The patient, a 3-month-old girl, was referred for investigations of convulsions, macrocephaly and delayed milestones. She was the only child of parents who were first cousins. She

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Address for correspondence: Dr P. J. Patel, X-ray Department (40), King Khalid University Hospital, PO Box 2925, Riyadh 11461, Kingdom of Saudi Arabia

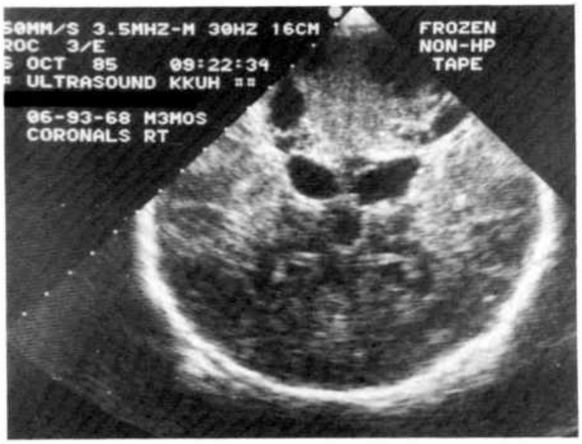

FIG. 1.
Coronal cranial sonogram showing diffuse leucomalacia and multiple anechoic areas in periventricular region.

was delivered at full term with no immediate or late neonatal complications. On examination, she had macrocephaly and the head circumference, at 45 cm, was above the 90th percentile. The anterior fontanelle was bulging and the cranial sutures were separated. She was not following objects and fundoscopic examination revealed bilateral pale discs. She had poor head and neck control and deep-tendon reflexes were hyperactive in all four limbs. Other systems were substantially normal. Cranial sonography showed multiple anechoic lesions in the cerebrum with increased sonolucency of white matter (Fig. 1). Cranial CT revealed diffuse, low-attenuation white matter distributed symmetrically throughout both hemispheres (Fig. 2). A brain biopsy from the right frontal lobe was taken for frozen section and microscopic examination showed a normal cortex. The deeper, gelatinous part showed cells which were almost all vacuolated, the vacuoles being multiple or single and often compressing the nucleus to one side (Fig. 3).

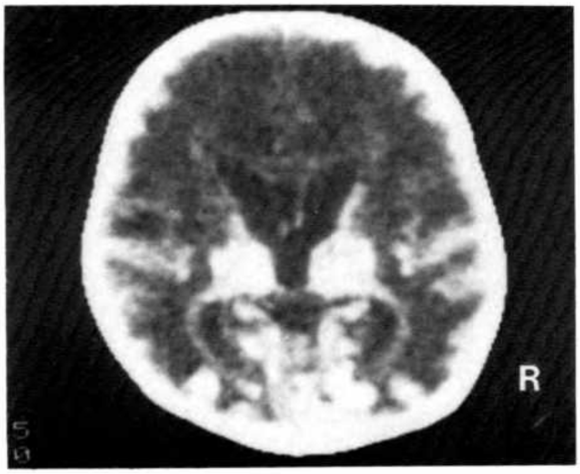

FIG. 2.
Axial CT scan showing diffuse, low-attenuation white matter in both hemispheres.

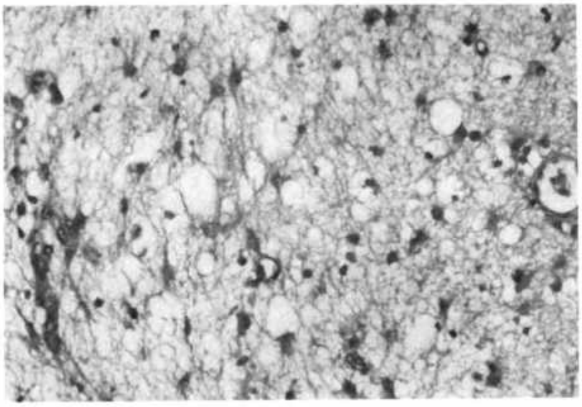

FIG. 3.
A photomicrograph of the spongy white matter from the biopsy specimen, showing numerous vacuoles throughout the tissue (haematoxylin and eosin, × 199).

The vacuoles were clear and did not show with fat stains in frozen sections. These changes were consistent with Canavan's disease.

DISCUSSION

Canavan's disease is a recessively inherited disorder of infancy, of unknown aetiology, demonstrating megalencephaly, blindness, initial hypotonia followed by spasticity and progressive psychomotor degeneration with onset between the second and ninth months of life (Seungho & Krishna, 1983). Boltshauser and Isler (1976) reported CT findings as diffuse, low-attenuation white matter distributed symmetrically throughout both hemispheres. Identical findings were present in our case.

Sonographic examination showed increased sonolucency of white matter with multiple, cavitary anechoic lesions due to lack of myelin and an increased water content in the affected areas. Similar findings have been reported in many conditions, *e.g.* asphyxia (Kesaree et al, 1976; Dubois et al, 1979), meningitis (Smith et al, 1977; Chutorian et al, 1979), twin-to-twin transfusion (Yoshioka et al, 1979; Claireaux, 1972), and ischaemic brain disease (Trounce & Milevene, 1985).

The outstanding pathological feature is spongy change predominantly affecting the white matter, with lack of myelin and an increased water content (Boltshauser & Wilson, 1976). These characteristic features were found in our case.

CONCLUSION

It is, therefore, pertinent to consider Canavan's disease in the differential diagnosis of intracerebral, multicystic leucomalacia from cranial ultrasound or low-attenuation, non-enhancing white matter on cranial CT. The disease can be definitely diagnosed only by brain biopsy.

REFERENCES

BOLTSHAUSER, E. & ISLER, W., 1976. CT in spongy degeneration. *Lancet*, *i*, 1123.

1986, *The British Journal of Radiology*, *59*, 1228–1229

Boltshauser, E. & Wilson, J., 1976. Value of brain biopsy in neurodegenerative disease in childhood. *Archives of Disease in Childhood*, *51*, 264–268.

Chutorian, A. M., Michener, R. C., Defendini, R. & Hilal, S. K., 1979. Neonatal polycystic encephalomalacia. Four new cases and review of the literature. *Journal of Neurology, Neurosurgery and Psychiatry*, *42*, 154–160.

Claireaux, A. E., 1972. Multicystic encephalomalacia. *Developmental Medicine and Child Neurology*, *14*, 662–663.

Dubois, P. J., Heinz, E. R., Wessel, H. B. & Zaias, B. W., 1979. Multiple cystic encephalomalacia of infancy: computed tomographic findings in two cases with associated intracerebral calcification. *Journal of Computer Assisted Tomography*, *3*, 97–102.

Kesaree, N., Poland, R. L. & Hart, Z. H., 1976. Encephaloclastic porencephaly: post-natal evaluation. *Journal of Pediatrics*, *88*, 598–599.

Seungho, H. L. & Krishna, C. V. G. R., 1983. *Cranial Computed Tomography*. Ed. by H. L. Seungho and C. V. G. R. Krishna (McGraw Hill Book Company, Maidenhead), pp. 669–670.

Smith, J. B., Groover, R. V., Klass, D. W. & Housen, O. W., 1977. Multicystic cerebral degeneration in neonatal herpes simplex encephalitis. *American Journal of Diseases of Children*, *131*, 568–572.

Trounce, J. O. & Levene, L. I., 1985. Diagnosis and outcome of subcortical cystic leukomalacia. *Archives of Disease in Childhood*, *60*, 1041–1046.

Yoshioka, H., Kadamoto, Y., Mino, M., Morikawa, Y., Kasabuchi, Y. & Kusunoki, T., 1979. Multicystic encephalomalacia in live-born twin with a still born macerated co-twin. *Journal of Pediatrics*, *95*, 798–800.

Cystic dilatation of the thoracic duct presenting as a supraclavicular mass

By A. Kolbenstvedt, M.D. and J. Aanesen, M.D.

Departments of Radiology and Otorhinolaryngology, Rikshospitalet, The National Hospital, Oslo, Norway

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Cystic dilatation of the mediastinal thoracic duct is an uncommon lesion. Emerson (1950) described the first case diagnosed at surgery during the patient's lifetime. He found four previous reports of supradiaphragmatic thoracic duct cysts diagnosed post-mortem, the first by Enzmann in 1883. Tsuchiya et al (1980) reviewed eight cases described since 1950 and added one case which they believed to be the first diagnosed before thoracotomy. That was a posterior mediastinal cyst shown by pedal lymphography and computed tomography. The majority of the supradiaphragmatic thoracic duct cysts appeared in the mediastinum, but one example lying in the left supraclavicular region was reported by Barlow and Gracey (1965).

CASE REPORT

A previously healthy 55-year-old man was referred to the department of otorhinolaryngology with an asymptomatic left supraclavicular mass discovered 7 months earlier. The mass was fluctuant, 3 cm in diameter and located lateral to the lower part of the sternocleidomastoid muscle (Fig. 1). Fine-needle puncture yielded white, milky fluid which, at microscopy, was found to contain protein and numerous lymphocytes. Biochemical analysis of aspirated fluid showed a cholesterol content of 2.0 mmol/l (reference values for serum 5.4–8.4 mmol/l) and a triglyceride level of 28 mmol/l (reference values for serum 0.6–2.4 mmol/l). These findings indicated chylous fluid.

Chest radiography was normal. At lymphography a total of 17 ml of Lipiodol (May & Baker) was injected in a pedal lymph vessel, the last 7 ml with the upper half of the body elevated in order to visualise the thoracic duct. Normal lymph vessels and nodes were demonstrated in the inguinal, pelvic and lumbar regions, but the thoracic duct was not demonstrated. Images from computed tomography were partly

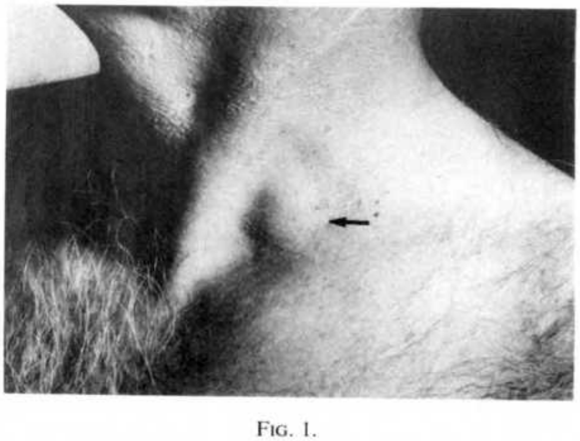

Fig. 1.

Photograph of the left supraclavicular region, showing a mass (arrow) behind lower part of the sternocleidomastoid muscle.

Correspondence to: A. Kolbenstvedt M.D., Department of Radiology, Rikshospitalet, 0027 Oslo 1, Norway.

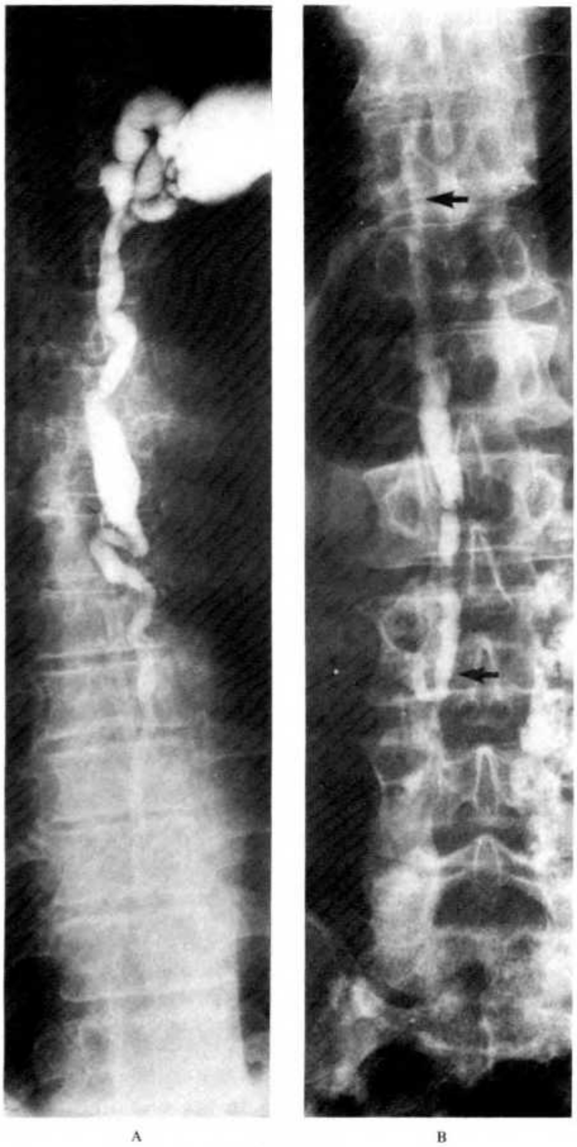

FIG. 2.

Radiography of the thoracic duct following direct puncture and injection of contrast medium into the supraclavicular cystic mass. (A) Tortuous upper part with cystic dilatation. (B) Lower part with cisterna chyli and lumbar trunk demonstrated down to the level of the third lumbar disc.

disturbed by artefacts due to the patient's broad shoulders. A cystic mass with attenuation value −26 HU was identified. At direct puncture 20 ml of non-ionic, water-soluble contrast medium (iohexol, 350 mg I/ml) was injected. The cyst was filled with medium and gradually a widened, tortuous thoracic duct, cisterna chyli and lumbar trunk were demonstrated down to the level of the 3rd lumbar disc (Fig. 2). No contrast medium passed to the subclavian vein, indicating obstruction of the thoracic duct inlet.

As the patient had no symptoms, he was not subjected to surgery. At follow-up examinations 14 months and 36 months later, the condition was unchanged.

DISCUSSION

Enzmann (1883) quoted by Emerson (1950) described a post-mortem finding similar to the present case. Near the upper end of the thoracic duct an egg-shaped, smooth cyst was found, with a clot plugging the entrance into the left subclavian vein. This cyst was assumed to be caused by mediastinitis. Barlow and Gracey (1965) described a 76-year-old woman with a gradually enlarging swelling in the left side of the neck of 2 years' duration. Surgery disclosed cystic dilatation of the thoracic duct containing clear fluid and communicating with the afferent thoracic duct, while a thin, fibrous membrane separated the distal end from the subclavian vein. The wall of the dilated part showed degenerative changes.

Ross (1961) recognised two varieties of duct cysts: the lymphangiomatous (congenital) and the degenerative (acquired). As obstruction by ligation will not cause a cystic dilatation, a combination of degenerative change and obstruction may be postulated as a cause for the non-lymphangiomatous acquired cysts. In our case, puncture with aspiration of fluid for biochemical analysis combined with injection of water-soluble contrast medium for radiological examination was an easy and direct procedure which allowed the diagnosis to be made without surgical intervention.

REFERENCES

BARLOW, D. & GRACEY, L., 1965. Cystic dilatation of the thoracic duct. *British Journal of Clinical Practice, 19*, 101–102.

EMERSON, G. L., 1950. Supradiaphragmatic thoracic-duct cyst. *New England Journal of Medicine, 242*, 575–578.

ROSS, J. K., 1961. A review of the surgery of the thoracic duct. *Thorax, 16*, 12–21.

TSUCHIYA, R., SUGIURA, Y., OGATA, T. & SUEMASU, K., 1980. Thoracic duct cyst of the mediastinum. *Journal of Thoracic and Cardiovascular Surgery, 79*, 856–859.

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Case reports

Hodgkin's disease during surveillance of Stage I testicular teratoma

By *M. D. Leslie, B.Sc., M.R.C.P., M. Brada, B.Sc., M.R.C.P., F.R.C.R. and M. J. Peckham, M.D., F.R.C.P., F.R.C.R.

Institute of Cancer Research and The Royal Mardsen Hospital, Downs Road, Sutton, Surrey SM2 5PT

(*Received March 1986*)

It has become an established practice in some specialised centres for patients with Stage I non-seminomatous germ-cell tumours of the testis to be kept under close surveillance following orchidectomy.

We report a patient with testicular teratoma treated with orchidectomy alone who, during the period of close observation, developed Hodgkin's disease.

CASE REPORT

The patient, a 20-year-old man, had an inguinal orchidectomy for left testicular enlargement which was histologically a malignant teratoma, undifferentiated. Initial chest radiography, lymphography and computed tomography (CT) of the chest and abdomen were normal. Serum alpha fetoprotein (AFP) and beta human chorionic gonadotrophin (BHCG) were undetectable. Monthly examinations, radiography marker estimation (AFP and BHCG) and 2-monthly CT scans remained normal for over a year. At 14 months an anterior mediastinal mass was demonstrated by both CT (Fig. 1) and chest radiography. Other investigations remained normal. Thoracotomy was performed to obtain a tissue diagnosis and it revealed an enlarged thymus which was completely excised. Histological examination showed nodular sclerosing Hodgkin's disease. On subsequent staging there was no disease detected outside the mediastinum and he was classified as clinical Stage IA (Ann Arbor staging). Following mantle radiotherapy he is well and free of both Hodgkin's disease and teratoma.

COMMENT

Following orchidectomy for testicular tumour, patients are carefully staged with chest radiography, lymphography, CT of chest and abdomen and measurement of serum AFP and BHCG concentrations. Careful surveillance has shown that more than 70% of Stage I patients remain disease-free and do not require further treatment (Peckham et al, 1982). The meticulous screening involved in such an approach occasionally leads to the detection of abnormalities which need to be distinguished from metastatic teratoma, particularly in the absence of raised serum marker levels. During the surveillance of 120 Stage I teratomas, six patients developed opacities shown by CT of the chest which did not represent teratoma. By CT criteria they were diagnosed in three patients as inflammatory, in two as benign pleural lesions and in a further patient as benign granuloma.

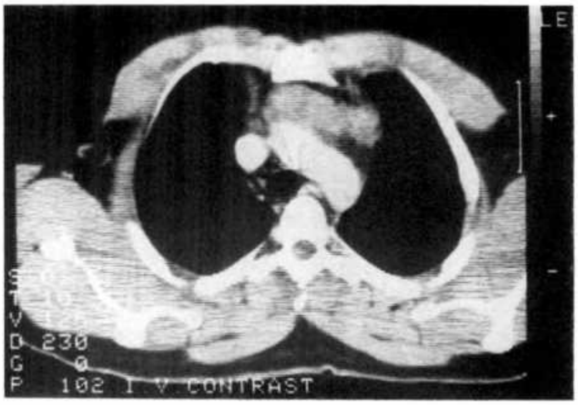

FIG. 1.

Section of the chest on CT showing an anterior mediastinal mass.

Involvement of the mediastinum, particularly in the absence of infradiaphragmatic lymph node disease, is an unusual pattern of spread for testicular teratoma and it was, therefore, considered imperative to obtain a histological diagnosis in the present patient.

Second tumours are increasingly reported in patients successfully treated for testicular tumours and are usually attributed to previous therapy. An excess of urinary and gastrointestinal tract tumours has been noted in patients with testicular tumours 15–19 years after radiation therapy (Hay et al, 1984). Development of leukaemia following both chemotherapy and radiotherapy for germ-cell tumours has also been described (Redman et al, 1984). Hodgkin's disease and non-Hodgkin's lymphoma have been reported both before (Cavalli et al, 1980) and after (Trump & Linet, 1980) the diagnosis of testicular tumour. To our knowledge, Hodgkin's disease following orchidectomy alone has not been described. The present observations emphasise the need for caution in ascribing second malignancies to previous therapy and also underline the importance of establishing a tissue diagnosis in patients under surveillance where serum marker levels are not raised and the pattern of spread appears unusual.

REFERENCES

CAVALLI, F., FASSLER, H., KAPLAN, S. & CAMPONOVO, F., 1980. Testicular cancer after treatment for Hodgkin's disease (letter). *New England Journal of Medicine*, *302*, 1478–1479.

HAY, J. H., DUNCAN, W. & KERR, G. R., 1984. Subsequent malignancies in patients irradiated for testicular tumours. *British Journal of Radiology*, *57*, 597–602.

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*Present address: The Royal Free Hospital, London.

PECKHAM, M. J., HUSBAND, J. E., BARRETT, A. & HENDRY, W. F., 1982. Orchidectomy alone in testicular Stage I non-seminomatous germ cell tumours. *Lancet, ii,* 678–680.

REDMAN, J. R., VUGRIN, D., ARLIN, Z. A., GEE, T. S., KEMPIN, S. J., GODBOLD, J. H., SCHOTTENFELD, D. & CLARKSON, B. D., 1984. Leukaemia following treatment of germ cell tumours in men. *Journal of Clinical Oncology, 2,* 1080–1087.

TRUMP, D. L. & LINET, M., 1980. Lymphoma and cancer of the testis (letter). *New England Journal of Medicine, 303,* 1063

Book review

Diagnostic Paediatric Imaging: a case study teaching manual. By C. M. Hall and S. Lingam, pp viii + 206, 1986 (Springer-Verlag, Berlin), £29.00.
ISBN 3–504–16202 (Berlin)
0–387–16202 (USA)

According to the preface, this book aims to be a teaching manual for candidates taking higher medical examinations and it succeeds in this aim. It will make the reader think along paediatric lines and there are good lists of differential diagnoses.

The layout is well arranged for self-tuition. Case illustrations together with a short clinical history and questions are placed on one page; answers and suggestions for further investigation by other suitable techniques are discussed on the back of the same page. This format makes it very easy to keep track of questions and answers.

The 100 cases are grouped in sections, gastrointestinal tract (23), genito-urinary system (13), respiratory and cardiovascular systems (22), central nervous system (five), endocrine system (five), and skeletal system (32). The selection is very much examination orientated and this is not the book for the casualty officer or the doctor on "acute take".

There are a few quibbles. The illustrations are not always clear. For instance, where is the Replogle tube in Case 9 or the lung plethora in Case 16? Does the diameter of the pylorus really have to be 2 cm before a diagnosis of pyloric stenosis can be made? (No, it does not.) Altogether, ultrasound is not given the prominence it merits. Surely polycystic disease of the kidneys should be diagnosed by ultrasound rather than intravenous urography. I think a list of recommended reading would have been useful.

The book will provide plenty of food for thought for examination candidates and be helpful in their studies.

G. M. STEINER

Book reviews

Quality Control Handbook Ed by S. Stockley, pp. 105, 1986 (ISRRT, Weybridge), £4 00
(No ISBN)

This publication is designed for the use of technicians, in radiography world-wide, using simple X-ray equipment and manual film processing. It was written following a quality control course in Harare in 1983 when technicians representing 11 African countries identified the need for such a book The book gives guidance to technicians who have some training in radiography and are keen to introduce quality control within their own departments It is designed as a teaching manual and the layout provides space for working notes to keep alongside the instructions. The three main sections of the book deal with setting standards for local working conditions, maintaining standards of quality and problem solving.

The first section on setting standards instructs the user on the preparation of the X-ray equipment and film processing which is required before commencing a quality control programme This includes general cleanliness, good working practices and mechanical and electrical safety.

The monitoring tests described for maintaining standards are all very useful tests which are simple to carry out and do not use complicated test tools. For example, the test to check consistency of the X-ray generator uses a water phantom and a meter rule. All the instructions are extremely clear and easy to follow, even for those technicians whose first language is not English. The problem-solving section provides a quick method of investigating and diagnosing faults

In total, the book provides a complete guide to the introduction of quality control in a simple yet comprehensive way. It is written specifically for those departments where expensive test tools and highly-trained personnel are not available, and proves that neither are essential. The book fulfils its purpose by meeting the needs of the radiographically developing world, but it will also be of use to any department where basic quality control has not yet been introduced. I am certain this book will be highly valued by radiographers and radiological technicians throughout the world

M J. HARVEY

Percutaneous and Interventional Urology and Radiology (Clinical Practice in Urology series). Ed. by Erich K. Lang, pp 362, 1986 (Springer-Verlag, Berlin), £74 00.
ISBN 3–540–15589–9 (Berlin)
0–387–15589–9 (USA)

The title given to this book takes no chances with definitions Previous expositions on the broad subject have, for example, been entitled *Endourology* or *Interventional Uro-radiology* This book lives by its title, covering nearly all aspects of modern urological and radiological diagnostic and therapeutic practice. Therein, however, lies a problem There are chapters in this book covering subjects only obliquely related to interventional or percutaneous techniques, but perhaps the book is none the worse for that.

Dr Lang has collected together 19 contributors including himself. It is heartening to see that the majority are radiologists! Percutaneous nephrostomy, ureteric stenting, upper tract dynamics and calculous disease are dealt with in the first third of the book No mention is made of laser technology applied to the urinary tract and not enough is made of the combination required of interventional procedures and shock-wave lithotripsy Excellent chapters on percutaneous drainage and aspiration biopsy of renal tract abscess and tumour then follow Regional chemotherapy is discussed, but is little used in the UK. There is no mention of prostatic biopsy under ultrasound control nor of radioactive seed implants, again under ultrasound control The pros and cons of transcatheter embolisation of tumours and varicoeles is covered, as is the diagnosis and treatment of haemorrhage from pelvic organs. Rather surprisingly, the final chapters of the book are devoted to the diagnosis of benign and malignant renal tumours and the diagnosis and assessment of renal inflammatory disease. Although well done, these chapters are out of place, having little input from interventional techniques

This book tries, perhaps, to do too much in too few pages and is not entirely faithful to its title. It is, however, beautifully written, well referenced and the illustrations are up to Springer's usual excellent standard. It should find a place on the shelves of an ever-growing number of departments involved in the modern aspects of urology and uroradiology.

DAVID RICKARDS

1986, *The British Journal of Radiology*, 59, 1233–1235 DECEMBER 1986

Case of the month

A painful scoliosis

By *P. G. Preston, B.Sc., M.R.C.P., F.R.C.R.

Department of Radiology, Edinburgh Royal Infirmary, Edinburgh

(*Received February 1985*)

A 14-year-old girl presented with a 2-year history of continuous pain in the lumbar region. The pain was worse at night, exacerbated by movement and partially relieved by analgesics. On initial examination she had a thoraco-lumbar scoliosis with severe restriction of all movements of the lumbar spine. Plain radiography of the spine (Fig. 1) demonstrated a thoraco-lumbar scoliosis, extending from T7 to L3, concave to the left with a Cobb angle of 31° and no other abnormality.

What is the differential diagnosis and what other investigations would be most helpful?

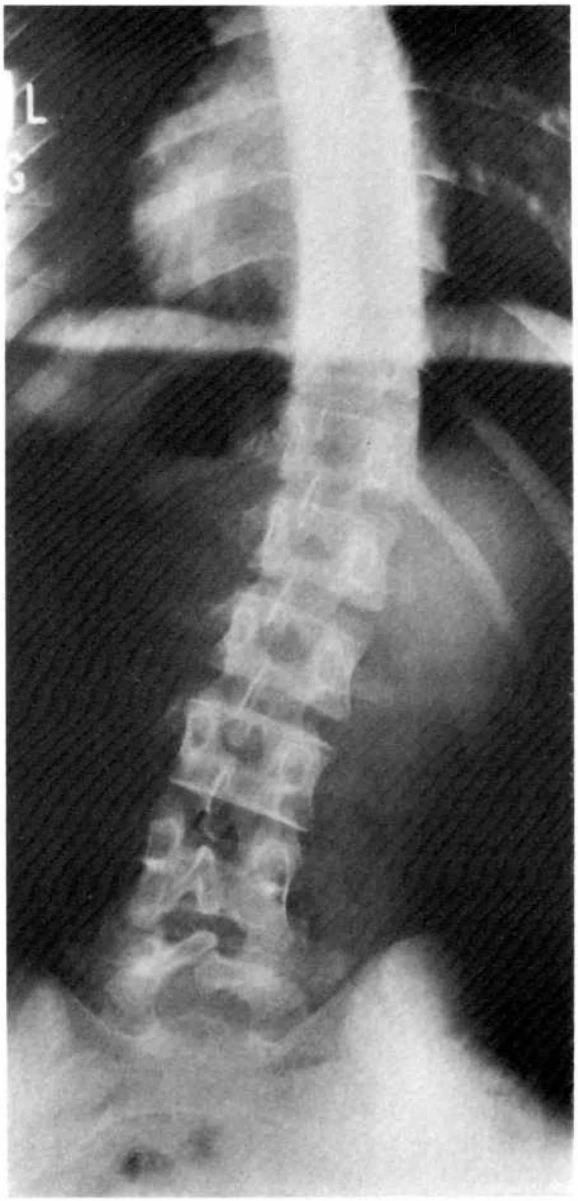

FIG. 1

Postero-anterior radiograph of the spine showing scoliosis and an unfused neural arch at L5, but no other abnormality.

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*Now at the Norfolk & Norwich Hospital.

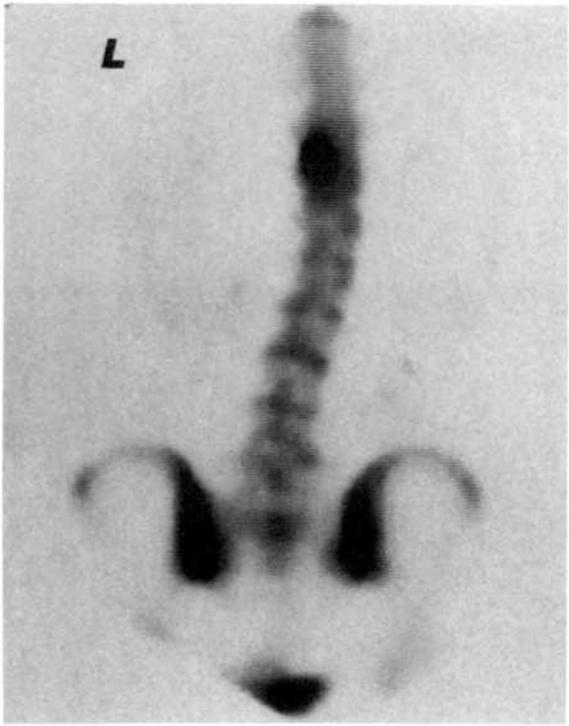


FIG. 2.
Isotope bone scan, posterior view. An area of increased activity is shown on the left at T11.

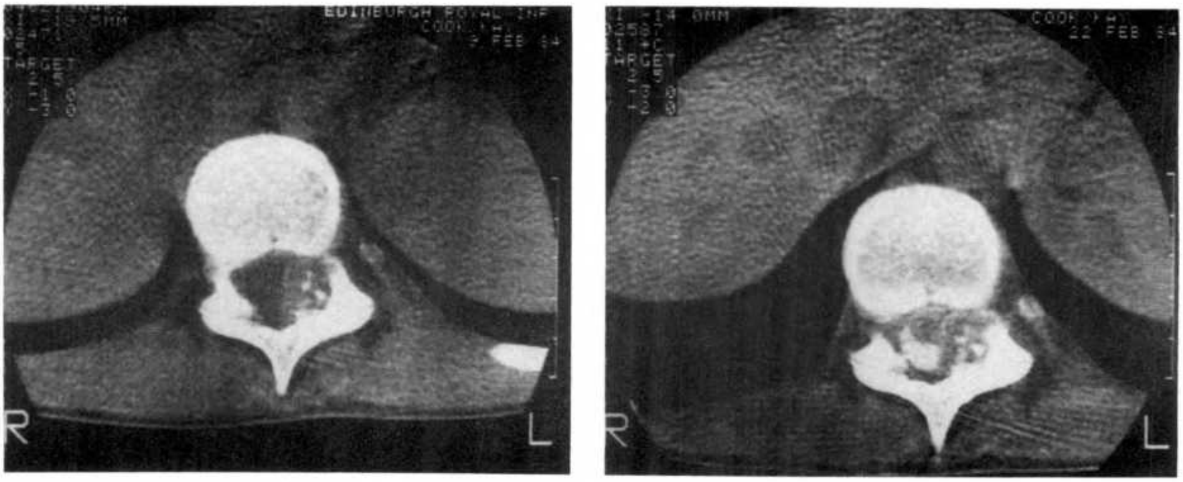
Adolescent scoliosis may be seen at this age, but is not painful, and the history of pain should raise the possibility of underlying pathology. Night pain and relief by analgesics is seen in osteoid osteomas and in osteoblastoma.

A bone scan (Fig. 2) was performed which showed a solitary area of increased uptake in the left side of T11, at the apex of the concavity of the scoliosis. Computed tomography was also performed at this level (Fig. 3) and showed a mass arising from the left pedicle of T11 and extending into the spinal canal, with displacement of the thecal sac to the right. The mass was of mixed attenuation, having calcification and soft-tissue densities within it.

At operation, a soft, red, lobulated tumour was found arising from the pedicle of T11 and extending into the spinal canal. The tumour was removed and an interfacet: intertransverse fusion was performed from T10 to T12. The tumour measured 3.2 cm × 1.5 cm × 1 cm. Histological examination showed immature woven bone and osteoid trabeculae within richly vascular connective tissue. There was little evidence of organisation around a central nidus. Her pain disappeared within 24 h of the operation. Her scoliosis progressively resolved and 6 months after surgery the angle of the scoliosis had decreased from 31° to 15°. After 12 months the Cobb angle measured 6°.

DISCUSSION

There is considerable difficulty clinically, radiologically and histologically in distinguishing osteoblastoma and osteoid osteoma when they occur in the spine. Clinically, an osteoid osteoma is often associated with more pain, which can be worse at night and may be relieved by aspirin. Radiologically, the major differentiation can be based on size and degree of reactive sclerosis. Osteoid osteomas have a limited growth potential, whereas osteoblastomas enlarge progressively



A

B

FIG. 3.
Computed tomography of the spine at T11, (A) without and (B) with intrathecal contrast medium (L + 100, W 500). A soft-tissue mass with calcified areas is extending into the canal from the left side of the neural arch and displacing the theca to the right.

and have dimensions usually greater than 1.5 cm. A tumour which grows and expands into the spinal canal is much more likely to be an osteoblastoma.

The location of both tumours in the spine is similar, usually in the neural arch in the region of the pedicle or base of the transverse process.

Characteristically, osteoid osteomas cause more reactive sclerosis. The CT scan usually shows this sclerosis surrounding a central nidus but in some cases only the reactive sclerosis is visible. Calcification and new bone formation within the tumour is more often seen in osteoblastomas (McLeod et al, 1976).

Histologically, an osteoid osteoma may show organisation around a central nidus, whilst an osteoblastoma shows mineralisation and large vascular spaces (Marsh et al, 1975).

Delay in the diagnosis of a spinal bone tumour is common but it should be suspected if there is a painful scoliosis (Kirwan et al, 1984). In a growing child, progression of the scoliosis with vertebral rotation may occur during this delay and subsequent surgical excision of the lesion may not result in complete resolution of the scoliosis (Ransford et al, 1984).

Plain radiography is positive in less than 50% of patients (Kirwan et al, 1984) and if CT is available, plain tomography is unnecessary. An isotope bone scan should be performed in all patients, this will be positive in almost 100% of patients with an osteoid osteoma (Lisbona & Rosenthall, 1979) and CT scans can then be performed at the appropriate level. The location and extent of the tumour are well demonstrated and the contrast resolution of CT allows better appreciation of calcification and new bone formation than does plain tomography

In summary, the case of a 14-year-old girl with a painful scoliosis and spinal stiffness is presented. The radiological investigations indicated that the most likely diagnosis was an osteoblastoma of the spine and this final diagnosis was made from the combination of radiological and histological findings.

REFERENCES

KIRWAN, E O'G., HUTTON, P A. N, POZO, J L & RANSFORD, A. O, 1984 Osteoid osteoma and benign osteoblastoma of the spine. *Journal of Bone and Joint Surgery, 66B*, 21–26.

LISBONA, R. & ROSENTHALL, L., 1979. Role of radionuclide imaging in osteoid osteoma. *American Journal of Roentgenology, 132*, 77–80

MARSH, B W., BONFIGLIO, M, BRADY, L. P & ENNEKING, W. F, 1975. Benign osteoblastoma: range of manifestations *Journal of Bone and Joint Surgery, 57A*, 1–9.

MCLEOD, R. A, DAHLIN, D. C. & BEABOUT, J. W, 1976. The spectrum of osteoblastoma. *American Journal of Roentgenology, 126*, 321–335

RANSFORD, A. O, POZO, J L., HUTTON, P. A. N. & KIRWAN, E. O'G., 1984 The behaviour pattern of the scoliosis associated with osteoid osteoma or osteoblastoma of the spine. *Journal of Bone and Joint Surgery, 66B*, 16–20.

1986, *The British Journal of Radiology*, 59, 1236–1238

Short communications

The use of the effective dose equivalent, H_E, as a risk parameter in computed tomography

By W. Huda, Ph.D. and G. A. Sandison, M.Sc.

Department of Medical Physics, Manitoba Cancer Treatment and Research Foundation, 100 Olivia Street,
Winnipeg, Manitoba R3E 0V9, Canada

(*Received April 1986*)

Conventional approaches to computed tomography (CT) dosimetry include the specification of the absorbed dose at given locations in the radiation field (Shope et al, 1982), the use of dose descriptors such as the Computed Tomography Dose Index (CTDI) (Shope et al, 1981), estimates of the total energy imparted in the CT examination (Huda, 1984) and an explicit evaluation of the somatic and genetic stochastic radiation risks associated with a given CT examination (Huda & Sandison, 1985) A problem with all these approaches is the difficulty of comparing the radiation risks associated with the CT procedure with the comparable risks associated with other diagnostic procedures that use ionising radiation. It is also difficult to compare the non-uniform radiation doses encountered in CT examinations with the whole-body dose-equivalent* limits imposed for non-medical exposures for members of the public (5 mSv/year) and for radiation workers (50 mSv/year), or with the risks from more familiar everyday activities such as smoking cigarettes and driving automobiles This note employs the concept of the effective dose equivalent, H_E, to overcome these problems. This parameter was introduced by the International Commission on Radiological Protection (ICRP, 1977a) to deal with partial-body radiation exposure of radiation workers Simple numerical radiation risk estimates from CT examinations performed on an EMI 5005 CT scanner are used to generate corresponding H_E values and this parameter is then adopted as the means for intercomparing total risk.

Effective Dose Equivalent, H_E

The ICRP has introduced the effective dose equivalent (ICRP, 1977a) which is defined by

$$H_E = \sum W_i H_i$$

where H_i is the mean dose equivalent in a given organ or tissue, i, and W_i is the corresponding weighting factor for organ i. Table I summarises the ICRP weighting factors which are considered appropriate for an adult working population where the risks for all organs (except the gonads) refer to cancer mortality and the gonad risk is the probability of serious genetic disorders in offspring in the first two generations. The interpretation of the value of H_E for a partial-body irradiation is that it corresponds to the same risk as a uniform whole-body radiation dose H_E, where the radiation risks are the induction of fatal cancers and serious genetic disorders in the first two generations. It is important to note that the use of H_E is only applicable at low radiation doses of the type normally encountered in diagnostic radiology and nuclear medicine, where the possibility of non-stochastic effects such as skin erythema and epilation is negligible.

H_E and CT Examinations

An explicit estimation of average radiation risks (genetic effects, fatal cancers and non-fatal cancers) for different types of CT examination performed with an EMI 5005 CT scanner has been reported elsewhere (Huda & Sandison, 1985) and a summary of these results is reproduced in Table II. To obtain an estimate of an effective dose equivalent, H_E, it is necessary to follow the recommended ICRP procedure (ICRP, 1977a) and neglect non-fatal cancers, taking into account the first two generations only and the age-dependent factor for producing children

These last two terms involve multiplicative factors of 0.5 and 0.4, respectively, to be applied to the sex-averaged genetic risk estimates shown in Table II Utilising the fact that a dose equivalent of 1 Sv corresponds to a total radiation risk of serious disorders of 1.65×10^{-2}, the values of H_E for each CT examination can be computed and these are shown in summary form in Table III

Discussion

Although the concept of the effective dose equivalent, H_E, was introduced by the ICRP for dealing with partial-body and non-uniform exposures in adult working populations, it is also very useful for estimating *average* risks in radiological procedures that employ ionising radiations. The estimation of such risks is the primary purpose of radiation dosimetry in

TABLE I

ICRP radiation risk estimates and weighting factors, W_i, for adult workers

Tissue	Radiation risk (Sv^{-1})	Weighting factor W_i
Gonads	4×10^{-3}	0.25
Breast	2.5×10^{-3}	0.15
Red bone marrow	2.0×10^{-3}	0.12
Lung	2.0×10^{-3}	0.12
Thyroid	5.0×10^{-4}	0.03
Bone surfaces	5.0×10^{-4}	0.03
Remainder	5.0×10^{-3}	5×0.06*

* A value of 0.06 assigned to five tissues not specified in table with highest radiation doses

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*The overwhelming majority of radiological procedures employ low-LET radiations and the dose equivalent (Sv) is for practical purposes taken to be equivalent to the absorbed dose (Gy).

TABLE II

SUMMARY OF RADIATION RISK ESTIMATES ASSOCIATED WITH CT EXAMINATIONS FOR AN EMI 5005 CT SCANNER

Scan type	Non-fatal cancers ($\times 10^{-6}$)	Fatal cancers ($\times 10^{-6}$)	Serious genetic effects in all future generations	
			Females ($\times 10^{-6}$)	Males ($\times 10^{-6}$)
Head	30.7	13.5	1.4	1.6
Chest	76	78.2	4.5	2.9
Pelvis	12.5	15.8	180	13
Abdomen	20.5	26.6	140	15

clinical radiology. The two difficulties that arise when using the concept of H_E for evaluation of patient exposures in clinical radiology are that the weighting factors given in Table I are only strictly applicable to adult working populations and that in many *individual* cases the average risk may significantly over- (or under-) estimate the true radiation risk because of the age or sex of the particular patient. For most practical purposes, the weighting factors for the population undergoing radiological investigations are unlikely to be markedly different from the values presented in Table I and any differences are likely to be considerably smaller than the uncertainties in the radiation risk estimates themselves. These radiation risk estimates are generally considered to have uncertainties corresponding to factors of 2–3 due to the range of values predicted by differing dose–effect extrapolation models and radiation risk models (National Academy of Sciences, 1980). The use of average risks as expressed by H_E, could thus be in sizeable error for individual patients such as children or post-menopausal women undergoing pelvic examinations (Table III).

However, explicit knowledge of the radiation risks are rarely required on an individual basis and are normally used for estimating the radiation detriment to populations or for intercomparing different imaging procedures that employ ionising radiations. In those specific cases where the computation of an individual radiation risk is desirable, it is possible to improve the precision of the risk estimates by reverting back to individual organ doses and using age and sex specific radiation risks that are available in the literature (ICRP, 1977b).

The values of H_E for the CT examinations shown in Table III indicate that head CT studies are associated with a H_E value of about 0.84 mSv which is comparable to the average annual whole-body background radiation dose equivalent to the population in the UK and in North America (United Nations Scientific Committee on the Effects of Atomic Radiation (UNSCEAR), 1982). The H_E value for chest CT examinations is relatively high at 4.78 mSv which reflects the high radiation doses received by the radiosensitive organs of the lungs, breasts and thyroid (Table I) and is approximately comparable to the current annual whole-body dose equivalent limit for members of the public. The average H_E value for pelvis and abdomen CT examination is about 2.4 mSv with approximately 50% of this H_E value due to the production of serious genetic disorders in the first two generations of an irradiated individual's offspring. In comparison, the genetic component of the value of H_E for head and chest examinations is negligible and reflects the relatively small radiation doses to the gonads for these examinations.

TABLE III

COMPUTATION OF H_E FOR DIFFERENT TYPES OF CT EXAMINATION ON AN EMI 5005 CT SCANNER

Scan type	Fatal cancer ($\times 10^{-6}$)	Average genetic effects ($\times 10^{-6}$)	Total serious disorders ($\times 10^{-6}$)	H_E (mSv)
Head	13.5	0.3	13.8	0.84
Chest	78.2	0.7	78.9	4.78
Pelvis	15.8	19.3	35.1	2.13
Abdomen	26.6	15.5	42.1	2.55

The values of H_E for CT examinations generated here can be directly compared with the corresponding values of H_E obtained in nuclear medicine examinations. The average value of H_E for 22 $^{99}\mathrm{Tc}^{m}$ procedures (Johansson et al, 1984) was 0.013 ± 0.010 mSv/MBq. Taking the typical $^{99}\mathrm{Tc}^{m}$ procedure to involve an administered activity of 370 MBq, the average value of H_E is 4.8 mSv, which is equal to the H_E value for a chest CT examination and a factor of six higher than a head CT examination performed on an EMI 5005 CT scanner.

The radiation risk estimates from radiological examinations as expressed by the value of H_E can be compared with the estimated risks of dying from lung cancer due to smoking cigarettes (1.4×10^{-7} death/cigarette) or dying in an automobile accident (5.6×10^{-8} death/mile driven) (Hall, 1978). On this basis, the current annual whole-body dose equivalent limit, H_E, of 5 mSv for members of the public is comparable to the risk from smoking 30 packs of 20 cigarettes or the risk in driving 1500 miles. It is important to use this type of intercomparison with a degree of caution due to considerable uncertainties associated with both the radiation and non-radiation risk estimates. They do, however, offer a useful yardstick that may be helpful as an educational aid both for the radiological profession and for members of the public.

REFERENCES

HALL, E. J., 1978. *Radiobiology for the Radiologist*, 2nd edit. (Harper & Row, Philadelphia).

HUDA, W., 1984. Is energy imparted a good measure of the radiation risk associated with CT examinations? *Physics in Medicine and Biology*, *29*, 1137–1142.

HUDA, W. & SANDISON, G. A., 1985. CT dosimetry and risk estimates. *Radiation Protection Dosimetry*, *12*, 241–249.

ICRP, 1977a. *Recommendations of the International Commission on Radiological Protection*. ICRP Publication 26 (Pergamon Press, Oxford).

1986, *The British Journal of Radiology*, 59, 1238–1240

——1977b. Problems involved in developing an index of harm ICRP Publication 27 *Annals of the ICRP, 1,* 12–14.

Johansson, L., Mattsson, S. & Nosslin, B., 1984. Effective dose equivalent from radiopharmaceuticals *European Journal of Nuclear Medicine, 9,* 485–489

National Academy of Sciences, 1980 *The Effects on Populations of Exposure to Low Levels of Ionizing Radiations* (Committee on the Biological Effects of Ionizing Radiations, Washington DC)

Shope, T. B., Gagne, R. M. & Johnson, G. C., 1981 A method for describing the doses delivered by transmission X-ray computed tomography *Medical Physics, 8,* 488–495.

Shope, T B., Morgan, T. J. Showalter, C. K., Pentlow, K S, Rothenberg, L N, White D R & Speller, R. D, 1982 Radiation dosimetry survey of computed tomography systems from ten manufacturers *British Journal of Radiology, 55,* 60–69.

UNSCEAR, 1982 *Ionizing Radiations Sources and Biological Effects*. Report to the General Assembly

A toxicity and pharmacokinetic study in man of the hypoxic-cell radiosensitiser RSU-1069

By *A. Horwich, Ph.D., M.R.C.P., F.R.C.R., *†S. B. Holliday, B.Sc., *†J. M. Deacon, M.Sc., M.R.C.P. and *M. J. Peckham, M.A., F.R.C.P., F.R.C.R.

*Royal Marsden Hospital and Institute for Cancer Research, Downs Road, Sutton, Surrey SM2 5PT and †Medical Research Council, Radiobiology Unit, Chilton, Didcot, Oxon OX11 0RD

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RSU-1069 is the principal member of a new group of hypoxic-cell radio- and chemo- ("mixed function") sensitisers. They contain both a 2-nitroimidazole ring similar to that of misonidazole and an aziridine ring which may function to bind the molecule to DNA (Adams et al, 1984, Walling et al, 1986) The compound was selected for clinical evaluation because of the high sensitiser enhancement ratio (SER) achieved following radiotherapy of hypoxic cells *in vitro* and in animal tumour studies (Adams et al, 1984), at 0.2 mM RSU-1069 the SER was 2.0 (cf 0.2 mM misonidazole, SER ≤ 1.6) and the concentration of RSU-1069 required to achieve an SER of 1.6 ($C_{1.6}$) was 7.5×10^{-5} M to 1×10^{-4} M (cf misonidazole $C_{1.6} = 3 \times 10^{-4}$ M) (Adams et al, 1984; Ahmed et al, 1986).

A toxicity study has been performed to define the tolerated single dose in man, and the plasma pharmacokinetics of RSU-1069 have been analysed in three patients treated at the high end of the dose range studied.

Patients and Methods

RSU-1069 (NSC 347503, 1-(2-nitro-1-imidazolyl)-3-(1-aziridinyl)-2-propanol) was prepared as previously described (Adams et al, 1984). It was supplied by the MRC Radiobiology Unit, Didcot, and stored in crystalline form at −20°C, shielded from light. Within 24 h of use, the required dose was dissolved in 100 ml of 0.1 M sodium bicarbonate solution and stored, shielded from light, at +4°C Administration was by a 17–19 min intravenous infusion. Having given full informed consent, seven patients received RSU-1069, three at a dose of 35 mg m^{-2}, three at a dose of 70 mg m^{-2} and one at a dose of 80 mg m^{-2} (see Table I). Plasma pharmaco-

TABLE I

Phase I study of RSU-1069 in seven patients

Patient age (years)	Diagnosis	Dose of RSU-1069 (mg m^{-2})	Toxicity	Duration (h)	Grade*
39	Teratoma	35	Nausea, vomiting	2	2
67	Adenocarcinoma, lung	35	None	—	0
57	Adenocarcinoma, lung	35	Nausea, vomiting	2	2
64	Squamous carcinoma, lung	70	Nausea, vomiting	2	3
33	Ewing's sarcoma	70	Nausea, vomiting	4	4
42	Teratoma	70	Nausea, vomiting	4	4
43	Liposarcoma	80	Nausea, vomiting	2	3

*WHO (1979)

kinetics were studied in the three patients treated with 70–80 mg m^{-2} doses Venous blood samples were taken before infusion and at periods afterwards for 1–24 h. Plasma was separated immediately by centrifugation and samples either kept on ice and analysed the same day, or stored frozen at −20°C

Pre-treatment assessments included full physical examination, laboratory tests of marrow, kidney and liver function and a chest radiograph. During and 2 h after the infusion, pulse and blood pressure were recorded at 15 min periods for 1 h and then at periods of 30 min. These were then recorded every 4 h for 24 h. The laboratory tests were repeated after 24 h and then weekly for 3 weeks Clinical assessment was repeated at 6 weeks

RSU-1069 was assayed by reversed-phase high-performance liquid chromatography (HPLC) on a Waters Associates Chromatograph. Separation was performed on a Waters Radial-PAK, μ BONDAPAK cyanopropyl (CN) cartridge, using a 10 mM $NH_4H_2PO_4$ buffer, pH 3, with a methanol gradient of 30–50% (Workman, personal communication, 1984) The compound was detected at 313 nm with a Waters model 440 absorbance detector

An aliquot of the injected drug solution was assayed at the time of treatment in three patients and no breakdown products were detected

Plasma levels were fitted to a two-compartment open model using a non-linear least-squares analysis (Sampson, 1970). The values obtained for the two-compartment model were corrected for the infusion period as described by Loo and Riegelman (1970) From the corrected values, the alpha- and beta-phase half-lives ($t_{1/2}$), total plasma clearance, area under the plasma concentration versus time curve (AUC) and steady-state volumes of distribution were calculated using the equations described by Wagner (1975).

Results

As seen in Table I, the major toxicity was gastrointestinal. Typically, the patient felt well for 2 h following the infusion, then severe nausea and frequent vomiting for approximately 2–4 h No symptoms attributable to the treatment remained the following day and thereafter There was no clinical or laboratory evidence of neurological, renal, hepatic, lung or cardiac damage.

Nausea and vomiting appeared refractory to antiemetic drugs The following were given by intravenous injection 30 min before the infusion of RSU-1069: 10 mg metoclopramide to two patients; 25 mg chlorpromazine to one patient; 12.5 mg prochlorperazine to one patient, 10 mg dexamethasone to one patient, and 10 mg dexamethasone and 25 mg chlorpromazine to one patient. Also, established nausea was treated with 10 mg intravenous metoclopramide or 12.5 mg prochlorperazine, and though nausea was not relieved within 1 h, it is not possible to be certain whether this symptom became less severe.

TABLE II

Plasma pharmacokinetics of RSU-1069 in three patients

Dose (mg m^{-2})	70	70	80
Total dose (mg)	140	126	136
Curve (Fig 1)	●	○	▽
Half-life (min)			
alpha phase	6.5	5 5	4.7
beta phase	123.3	69 3	67.2
AUC (μg ml^{-1} min m^{-2})	180.2	276.9	202 7
Clearance (ml min^{-1} m^{-2})	194 3	140.4	232 1
Volume of distribution (l m^{-2})	30.0	12.5	21.3

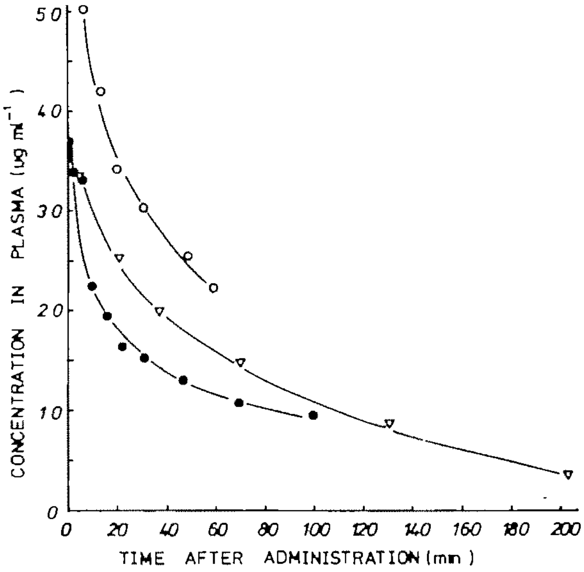

Fig. 1

Fall in plasma level of RSU-1069 in three patients following 15 min intravenous infusions ● 70 mg/m^2, ○ 70 mg/m^2, ▽ 80 mg/m^2 (1 M RSU-1069 = 212 gl^{-1})

The plasma pharmacokinetics following infusion of RSU-1069 were investigated in three patients The fall in plasma level was biphasic (Fig 1) with a $t_{1/2}$ alpha of 4.7–6.5 min and a $t_{1/2}$ beta of 67–113 min (see Table II). The calculated total area under the plasma concentration curve ranged from 180 to 277 mg ml^{-1} min m^{-2}.

The plasma concentration curves would indicate that following the initial distribution phase, levels of approximately 10–20 μM RSU-1069 were maintained for 20–40 min, this phase occurring approximately 15 min after infusion

Discussion

This study has demonstrated a dose-limiting toxicity of the mixed function hypoxic-cell radiosensitiser RSU-1069. This toxicity consisted of nausea and vomiting which was severe at a dose of 70 mg/m^2. This dose achieves a plasma level 30 min after infusion of approximately 10–20 μM and extrapolating from *in-vitro* data, this would correspond to a SER in hypoxic cells of only 1.2 (Adams et al, 1984) In the clinical context of fractionated radiotherapy, allowing reoxygenation and considering the unimpressive clinical results of the use of misonidazole with radiotherapy, it is extremely unlikely that this degree of radiation enhancement would be demonstrably useful (Brown, 1984).

The SER in tumours would be higher if there was selective uptake of RSU-1069. An initial report based on a study of KHT tumours in C3H/He mice suggested the contrary, with a tumour concentration only 29% of that of plasma over the

20–90 min following intraperitoneal injection (Workman & Walton, 1984). However, a study on the B16 melanoma in C57 Black mice has shown selective tumour uptake both for RSU-1069 and for the analogues RSU-1164 and RSU-1172 (Deacon et al, 1986). Tumour-to-plasma ratios of 3.7–4.0 were demonstrated with these drugs. Selective uptake in normal tissues was not found and, in particular, the brain-to-plasma ratio with RSU-1069 was less than unity. The explanation for the difference between these reports is not clear, and it may be that a selective uptake only occurs in certain tumours. RSU-1164 and RSU-1172 are less toxic than RSU-1069 in mice and will be investigated further, with a view to clinical studies (Ahmed et al, 1986).

RSU-1069 may have clinical applications in oncology other than as a radiosensitiser. Nitroimidazoles have been shown to potentiate the antitumour effects of alkylating agents *in vivo* (Rose et al, 1980); for example, in mice bearing intramuscularly-implanted MT tumours, RSU-1069 has been found to be the most effective potentiator of Melphalan when compared with a range of other nitroimidazoles (Sheldon et al, 1982, Adams et al, 1984). Also, RSU-1069 is a potent hypoxic-cell cytotoxin (Ahmed et al, 1986); it has been shown to be approximately 100 times more toxic to hypoxic than aerobic cells *in vitro*. Manipulation of the degree of tumour hypoxia using drugs which displace the oxyhaemoglobin dissociation curve (Adams et al, 1986) may further increase the therapeutic ratio from this approach.

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REFERENCES

Adams, G. E., Ahmed, I., Sheldon, P. W. & Stratford, I. J., 1984. Radiation sensitisation and chemopotentiation: RSU-1069, a compound more efficient than misonidazole *in vitro* and *in vivo*. *British Journal of Cancer, 49,* 571–577.

Adams, G. E., Barnes, D., du Boulay, C., Loutit, J., Cole, S., Sheldon, P., Stratford, I. J., van den Aardweg, G. J. M. J. & Hopewell, J., 1986. Induction of hypoxia in normal and malignant tissues by changing the oxygen affinity of haemoglobin. *International Journal of Radiation Oncology, Biology, Physics,* in press.

Ahmed, I., Jenkins, T. C., Walling, J. M., Stratford, I. J., Sheldon, P. W., Adams, G. E. & Fielden, E. M., 1986. Analogues of RSU-1069: radiosensitization and toxicity *in vitro* and *in vivo*. *International Journal of Radiation Oncology, Biology, Physics, 12,* 1079–1081.

Brown, J. M., 1984. Clinical trials of radiosensitizers: what would we expect? *International Journal of Radiation Oncology, Biology, Physics, 10,* 425–429.

Deacon, J. M., Holliday, S. B., Ahmed, I. & Jenkins, T. C., 1986. Experimental pharmacokinetics of RSU-1069 and its analogues: high tumour/plasma ratios. *International Journal of Radiation Oncology, Biology, Physics, 12,* 1087–1090.

Loo, J. C. K. & Riegelman, S., 1970. Assessment of pharmacokinetic constants from post infusion blood curves obtained after iv infusion. *Journal of Pharmaceutical Sciences, 59,* 53–55.

Rose, C. M., Millar, J. L., Peacock, J. H., Phelps, T. A. & Stephens, T. C., 1980. Differential enhancement of melphalan toxicity in tumour and normal tissue by misonidazole. In *Cancer Management Vol. 5. Radiation Sensitizers: Their Use in the Clinical Management of Cancer.* Ed. by L. W. Brady (Masson, New York), pp. 250–256.

Sampson, J., 1970. Non linear squares program BMDX 85. In *BMD Biomedical Computer Programs X-series Supplement.* Ed. by W. J. Dixon (University of California Press, Berkeley, California), pp. 177–186.

Sheldon, P. W., Batten, E. L., Scottow, D. J. & Adams, G. E., 1982. Potentiation of melphalan activity against a murine tumour by nitroimidazoles. *British Journal of Cancer, 46,* 525–531.

Wagner, J. C., 1975. *Fundamentals of Clinical Pharmacokinetics* (Drug Intelligence Publications, Hamilton), p. 82.

Walling, J. M., Stratford, I. J., Adams, G. E., Silver, A. R. J., Ahmed, I., Jenkins, T. C. & Fielden, E. M., 1986. Studies on the mechanism of the radiosensitising and cytotoxic properties of RSU-1069 and its analogues. *International Journal of Radiation, Oncology, Biology, Physics, 12,* 1083–1086.

WHO, 1979. WHO handbook for reporting the results of cancer treatment. *WHO Offset Publication No. 48.*

Workman, P. & Walton, M. I., 1984. Pharmacology of the mixed-function radio- and chemosensitizers CB-1954 and RSU-1069. *International Journal of Radiation Oncology, Biology, Physics, 10,* 1307–1310.

1986, *The British Journal of Radiology*, 59, 1241–1242 DECEMBER 1986

Correspondence

(The Editors do not hold themselves responsible for opinions expressed by correspondents)

Intracranial Hodgkin's disease: a primary presentation and access of cytotoxic agents

THE EDITOR—SIR,

Further to the report by Blake et al (1986), we have also seen two cases of intracranial Hodgkin's disease in this department during the past year. One was a primary presentation in a 62-year-old man, occurring as a solitary right fronto-temporal mass. Ten months after complete excision and whole-brain irradiation he is alive and free of systemic disease and intracranial recurrence (Ashby et al, case report in preparation). Histological examination showed this to be nodular sclerosing Hodgkin's disease (Grade I lymphocyte and histiocyte predominant subtype). The second case is reported briefly below to illustrate two interesting aspects.

An 18-year-old girl presented in March 1985 with Stage IIB nodular sclerosing Hodgkin's disease. She had right supraclavicular and pre-tracheal lymphadenopathy. Chest radiography showed widening of the mediastinum and nodal disease was confirmed at this site with computed tomography (CT); CT of the abdomen and pelvis, staging laparotomy and bone marrow examination were negative. She was managed with mantle irradiation.

She remained well until December 1985 when she returned with right-sided sciatic pain and subcutaneous nodules in the pre-auricular region. These were biopsied, and recurrent disease was confirmed. While she was being staged she was admitted as an emergency case after a grand mal convulsion. On examination she had evidence of L5/S1 right-sided root compression, but no other focal neurological signs. A firm mass, diameter 5 cm, was noted on the vertex of the scalp. Cranial CT showed a brightly enhancing mass adjacent to the skull vault high in the left parietal region, compressing underlying brain with some associated white-matter oedema (Fig. 1). There was also a similarly brightly enhancing soft-tissue extracranial lesion overlying the same site. The skull vault was intact at bone settings. Skull radiographs showed no bony erosion. Abdominal CT revealed extensive nodal recurrence, with right lower para-aortic and iliac extension associated with destruction of the tip of the transverse process of L5 and obliteration of fat within the spinal canal. No tumour cells were identified within the cerebrospinal fluid on cytospin examination, but a single intrathecal injection of methotrexate (10 mg) was given at this first diagnostic lumbar puncture. She was treated with combination chemotherapy (ChLVPP), and after three courses there was considerable regression of the intracranial lesion (Fig. 2) and the extracranial lump had disappeared. Cranial irradiation has been withheld, but will be considered to consolidate central nervous system (CNS) response if she achieves complete remission at other sites, or for progressive CNS disease. She is presently well and free of symptoms and continuing to receive chemotherapy.

There are two points worthy of note in this case. The first is the presence of a scalp mass with a meningeal mass underlying it, with normal bone between the two, suggesting that spread

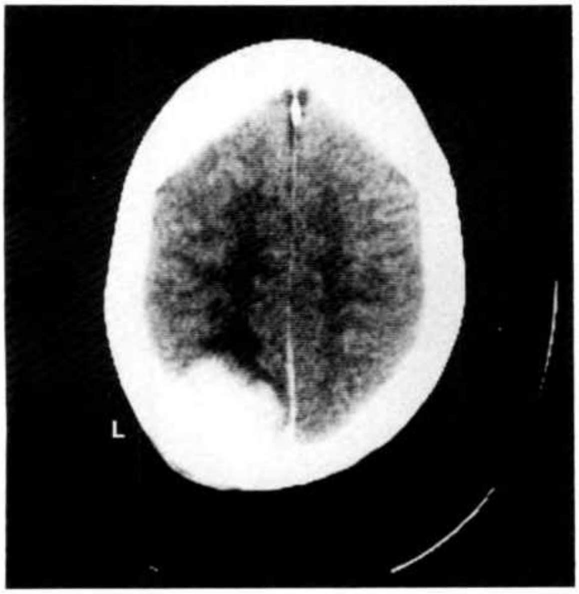

FIG. 1.

CT scan showing intracranial mass and soft-tissue extracranial lesion overlying the same site.

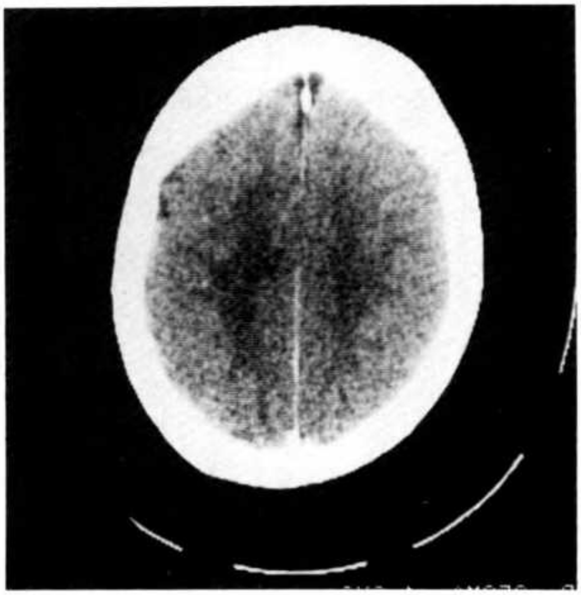

FIG. 2.

CT scan after three courses of chemotherapy.

has occurred through the emissary veins of the skull, although the direction of spread is not known. Secondly, cytotoxic drugs were almost certainly able to gain access to the meningeal tumour, either by the same route or as a result of disruption of the blood–brain barrier It seems very unlikely that 10 mg of intrathecal methotrexate would have produced such a response.

Yours, etc ,
M. A Ashby
D Bowen
J. V Watson

University Department of Clinical Oncology and Radiotherapeutics,
University of Cambridge School of Clinical Medicine,
Addenbrooke's Hospital,
Hills Road,
Cambridge CB2 2QQ
(*Received June 1986*)

REFERENCE

Blake, P R , Carr, D H. & Goolden, A W. G., 1986. Intracranial Hodgkin's disease. *British Journal of Radiology, 59,* 414–416.

Proposal to withdraw Min R film

The Editor—Sir,

It is a matter of great concern to us that we learnt from a circular distributed by Messrs Kodak Limited in August 1986 of their intention to discontinue the supply of Kodak Min R film for mammography from the end of 1986. Our paper (Kirkpatrick & Law, 1987) reports a study which confirms previous work indicating that, of available black and white films for mammography, Min R film currently represents the best balance between image quality and dose Subsequent work by us on Ortho M and PE 205, which are offered by Kodak as replacements for Min R, produced poorer image quality (Kirkpatrick & Law, 1987, addendum).

It is unfortunate that notice of withdrawal of this film coincides with publication of data showing it to be the most suitable for mammography It should also be noted that removal of Min R film from the market will increase the gulf between the performance of Medichrome Blue film and its nearest black and white rival, thereby considerably strengthening the argument for the use of Medichrome film despite the complications of different processing chemistry and viewing conditions.

We would urge those who are regular users of Min R film to communicate their feelings direct to the company

Yours, etc.,
A. E. Kirkpatrick
*J Law

Department of Radiology,
Royal Infirmary,
Edinburgh, and
*Department of Medical Physics and Medical Engineering,
Edinburgh University and Western General Hospital,
Edinburgh
(*Received September 1986*)

REFERENCE

Kirkpatrick, A. E & Law, J., 1987. A comparative study of films and screens for mammography. *British Journal of Radiology, 60,* in press

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*Authors' names spelt incorrectly in text.

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BIR Bulletin

December 1986

New Editor for the Journal

Dr Nicolas J. McNally takes over from Dr John Haybittle as non-medical Editor of *The British Journal of Radiology* with effect from January, 1987.

Nic McNally is well known as a radiobiologist with a wide range of interests both in his subject and outside it. From Dartington School in Devon he went to Bristol University where he obtained a B.Sc. (2i) in physics in 1962, adding a Postgraduate Certificate in Medical Physics in 1963. He then studied radiobiology under Dr Neil Gillies at the Middlesex Hospital Medical School, obtaining the M.Sc. in Radiation Biology and Radiation Physics of London University.

In 1965 he went to work at the MRC Experimental Radiopathology Research Unit at Hammersmith Hospital, under the eagle eye of Dr Tikvah Alper, and he obtained his Ph.D. while working there. Dr Alper has remained a strong influence on his radiobiological thinking, as indeed on the thoughts of many other scientists. While at the MRC unit he became an expert in animal-tumour radiobiology, developing from Dr Hugh Thomlinson's rat tumour a line of cells which would grow equally well in culture dishes or when implanted subcutaneously into rats as a tumour. There are still only a few such animal tumours available in the world. He set out to correlate cell survival after radiation treatments with factors that could be observed in the tumours *in situ*, such as regrowth delay. He investigated the effects of X rays, neutrons, hypoxia, and phase of the cell cycle on sublethal and potentially-lethal damage, among other projects.

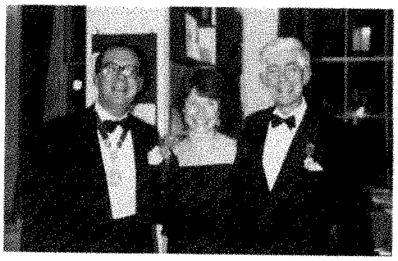
In 1972 he went to the Gray Laboratory of the Cancer Research Campaign at Mount Vernon Hospital, where he is now the Head of the Tumour and Cellular Radiobiology Section, and also the Animal Curator. He extended his techniques to other animal tumours, to radiosensitisers, chemosensitisers and combinations of neutrons and X rays. More recently he has been placed in charge of the flow cytometer at the Gray Laboratory and has developed a rapid assay for human tumour-cell proliferation rate, in collaboration with Dr Dische at Mount Vernon Hospital, using the monoclonal antibody to the DNA precursor BUdR. He has supervised and collaborated with many visiting workers from overseas and is much in demand as a lecturer both in this country and abroad. He is currently the Secretary of the Association for Radiation Research.

As well as all these scientific activities, Nic McNally and his family have a wide circle of friends in musical, theatrical and other circles. Nic is also a natural sportsman, being a squash ace until recently and a strong cricketer still.

He brings to his editorial responsibilities not only a wide range of scientific knowledge, but also a very sensible approach to practical problems. He has been a Deputy Editor of the *BJR* since 1981 and an Associate Editor before that.

President's dinner

The BIR President's Dinner was held in the Library of the Institute on the evening of Thursday, September 25. Council members and their partners attended for the speeches, buffet supper and the handing over of the badge of office to Professor Roger Berry by Professor Peter Wells, who in return was given his Past President's medal.



Miss Susan Johnstone, General Secretary, with Professors Berry (left) and Wells.

Obituary

George Richard Newbery, O.B.E., F.Inst. P.

Dick Newbery, for 23 years manager of the physics department and senior radiological safety adviser at the Radiochemical Centre, now Amersham International, died suddenly on June 12 this year at the age of 66.

Dick Newbery began his professional career during the war at the Army Radar Establishment at Malvern (later RRDE). After the war he joined the Medical Research Council (MRC) as a radiation physicist, becoming Senior Physicist at the MRC Radiotherapeutic Research Unit at Hammersmith Hospital. During this period the main need in radiotherapy was to develop X-ray machines to work at energies higher than 250 kV, which was the standard energy for deep ray treatment. The MRC decided to support the development of linear accelerators in collaboration with Metropolitan Vickers Ltd and Dick Newbery was appointed to represent the MRC in the project. With Paul Howard-Flanders, he invented the principle of isocentric mounting for therapy machines, now used universally. The prototype machine was installed in the MRC Unit at Hammersmith Hospital in 1953. The success of the linear accelerator as the main instrument for modern radiotherapy is in a large measure due to Dick's ability and hard work.

When the MRC cyclotron started working in 1955, Dick transferred most of his efforts to the production of radionuclides and to measurements of the neutron beam. In 1959 he left his post at Hammersmith to join the Radiochemical Centre at Amersham as manager of the physics department.

By this time the Radiochemical Centre had become established as the UK centre for commercial exploitation of radionuclides and was already the world's leading exporter of radionuclides, with 60% of its production going to customers overseas. Production was expanding rapidly and Dick quickly channelled his energies into the technical and commercial developments needed to support the expanding organisation.

Within his own department he developed expertise in methods for accurately calibrating a wide variety of radionuclides and introduced calibrated solutions of radionuclides as a commercial product line. He also built up a team to exploit rapidly-developing electronics technology to supply the needs of the production and development teams for sophisticated instrumentation. Over the next 20 years, state-of-the-art and, often, unique instruments were invented to back up the rapid technical developments in other areas of the Centre's operations. Last, but not least, Dick developed and strengthened his department's influence in all matters relating to radiological safety. The safe operation of the company's very varied production processes owes much to Dick's foresight.

Dick Newbery did not confine his interests to his own department. He became thoroughly immersed in all aspects of the Centre's work. He was deeply involved in the project to install the first radionuclide-producing cyclotron at the Centre. This machine was installed in 1965 and continues to produce radionuclides to this day, on a remarkably high duty cycle. Dick's career lasted to see the introduction of the company's second radionuclide-producing cyclotron in 1982. He was also closely associated with two other major developments which had lasting influence; the planning and introduction in 1968 of the Centre's first computer system for processing incoming orders, and the planning and development of the company's second major manufacturing site, at Cardiff, which began operation in 1979. He was awarded the O.B.E. in 1979 and retired in 1983.

Dick Newbery's professional career spanned periods of very rapid technical development in the organisations for which he worked. That the projects with which he was involved have been outstandingly successful is a tribute to Dick's integrity, ability and hard work. In addition to his scientific skills, he was an excellent organiser and administrator.

A. McNair

The International Working Party for the Diagnosis and Treatment of Cancer of the Cervix in Developing Areas

This informal association of radiotherapists, gynaecologists and physicists from industrialised and developing areas was formed in New York in 1971 at a congress discussing the hazards associated with the use of sources of radium 226, which was chaired by Dr Norman Simon of Mount Sinai Hospital, New York. At that time, increasing appreciation of these hazards had shown us the need to change to substitute sources and afterloading techniques: the need for this improved technology in developing areas was included in the full name of the Working Party. Increased and improved facilities for diagnosis and treatment were particularly important in developing areas where the disease is especially common among women in low socioeconomic groups, and where early marriage, multiparity and other factors important in the aetiology of this disease are prevalent, diagnosis is almost always late and treatment often not achieved at all. Radiotherapists from Mexico, South America, India, Yugoslavia, Egypt and Nigeria were all working to alert their public and governments to the importance of this disease and the possibilities offered by its adequate and early treatment, which clearly must be available on a national scale, and the International Working party was formed in order to assist in this effort. To do this we planned to meet regularly in developing countries at the invitation of one of our members and his association.

In 1972 about 30 of us met at the WHO in Geneva and since then we have met every two years: we have been to Rio de Janeiro, Hyderabad (India), Belgrade and Kladova, Cairo, Istanbul, Mexico City, Bangkok and ChiangMai. Our ninth meeting, on January 23, 1987, will be held in Calcutta at the invitation of Dr Saroj Gupta and the West Bengal Branch of the Indian Radiological and Imaging Association.

Oncologists from 43 countries have attended our eight meetings—150 delegates in Thailand included 100 members of the Working Party from 22 countries. The Working Party remains independent of other bodies, although it is sponsored scientifically by the WHO and the IAEA. There are no official delegates and any expert with interest and experience in any aspect of the problems of carcinoma of the cervix is welcome at any meeting. Reports on our meetings are sent to the WHO and the IAEE, which have often participated: a full report of the proceedings of the eighth (Thai) meeting was edited by Dr R. F. Mould with the assistance of Dr Kawee Tungsubutra and Dr Mould will be editing the report of the Calcutta meeting in collaboration with Mr A. Bose of Calcutta.

Over the years we have developed the pattern of our meetings. The members of the Working Party meet as a round table: 100 or more face each other at a circle of tables filling the room and discuss a wide variety of matters; papers are sent in and printed in advance but are not read in detail, and since they are already available and all members are experts, discussions are as spontaneous as possible and illustrated by slides. The chairmen at Calcutta will be Dr Margaret Snelling, London, Dr Daniel Chassagne, Villejuif, and Dr Saroj Gupta, Calcutta. Since the sad loss of Dr Norman Simon, founder member, in 1985, his place has been taken by Dr Chassagne. The subjects for discussion and the location of the next meeting are decided by the members at the first and last sessions.

Since the first meeting, in Rio de Janeiro, the round table has been followed by an "Encuentro" or international conference organised by the host. At this we are joined by oncologists of all kinds including administrators and public health experts, as well as surgeons and family doctors, pathologists, physicists and statisticians, etc. They come from centres all over the host country and neighbouring countries, for instance in 1987 the South-East Asia Regional Office of the WHO are publicising the Calcutta meeting and assisting delegates to attend in the 10 countries in their region which may adopt the methods to be discussed. At this conference there are didactic lectures and discussions planned to cover topics of special regional importance: in Calcutta the subject of the conference will be the plight of the village woman with carcinoma of the cervix in South-East Asia. Papers and reports from both meetings are published in the proceedings.

The International Working Party, in spite of meeting only in distant, developing areas and its interest in international health, has no funds, and many of us believe that this has encouraged our independent and active meetings. We have always agreed that members from industrialised countries will cover their own travel and hotel expenses without assistance from the agencies, but the regional agencies of the WHO may be able to assist some delegates nominated to attend the meetings, as is being done by the South-East Asian Regional Office for the Calcutta meeting.

It is our pride that there is no registration fee for our meetings, but of course we owe a great deal to our local hosts and their friends.

At our previous meetings we received generous assistance from a number of firms interested in brachytherapy, which participate in the meetings and also demonstrate and explain their wares. Amersham International plc, Buchler GmbH, CGR/Oris, Nucletron Trading BV and Sauerwein GmbH all supported the Thailand visit where they helped our running expenses significantly, as well as helping to publish the proceedings within the year and the posting of 133 volumes to the delegates.

IAEA/WHO project in Egypt

Discussions at meetings in which we were joined by Dr Racoveanu of Geneva and Dr Chris Taylor of Vienna stimulated much interest and inspired a combined IAEA/WHO project in Egypt where, generously financed by the Italian Government and supported by the Egyptian Government, Dr Mahfouz, as Director, is developing a national scheme for early diagnosis and treatment, near the patients' homes, of women with carcinoma of the cervix. With a central reference laboratory in Cairo University and five peripheral laboratories covering the country which receive slides and information from 19 collecting stations, a cytology smear service includes all women between 25 and 60 years old seen in those hospitals. At the same time, and based on the Nemrock Hospital at Cairo University, a network of five university, six general and seven district hospitals collaborate in creating new brachytherapy treatment centres in these hospitals, where teams of radiotherapist, gynaecologist and physicist are provided with afterloading sources of caesium 137 (Amersham/Manchester system). Protocols agreed by an IAEA/WHO advisory committee define the stages of the disease, the management of the patients and the exact technique to be used. Full details of clinical data, treatment and results will be collected and analysed in Cairo together with the results of the cytological smear service. It is hoped that this project, which will last for six years altogether, will be followed by similar projects in other countries and that the Working Party may later also consider the problems of accessible squamous-cell carcinoma in the oral cavity and skin and penile carcinoma.

In 15 years many subjects have been discussed at our round tables: we started with radioprotection and the hazards associated with the use of radium 226: there has been some improvement in the world since then, but all radium has not yet been withdrawn and substitutes supplied. Early discussions covered the gradual introduction of cobalt 60, caesium 137 and iridium 192 and we spent many hours discussing the sources available, the properties of the ideal afterloaded applicator and the dosimetry achieved, using manual and remote techniques. We talked of the advantages and disadvantages of conventional and high dose-rate therapy and of all aspects of dose, time and fractionation. We have discussed the development of a national oncology service, the place and work of university, regional and district hospitals, the organisation and training of diagnostic and training services and the equipment required. Recently there has been increasing talk of the place of the primary health service in the diagnosis and treatment of early cancer.

An international workshop to consider the place of high dose-rate therapy was held in London in 1978 by members of the Working Party who had used these techniques, and the second workshop was held in Giessen this year, chaired by Professor Helmut Vahrson of the Justus-Liebig University. This important and exact technique has significant advantages for patients and staff in the crowded centres in developing countries.

Invitation to new members

Many of us attend these meetings regularly, as we have found in them that ideal atmosphere best available in a small meeting of friendly international experts all concentrating on a small group of well understood problems. We have all learnt a great deal from each other and believe that together we have advanced the spread of modern brachytherapy in developing areas and that this will be followed by the development of full radiotherapy departments with teletherapy and multidisciplinary oncology available to all.

We welcome to our meetings graduates or technicians with experience as experts in the subject. Information is available through any of the chairmen: Dr Margaret Snelling, 7 Elm Place, London SW7, England, Dr Daniel Chassagne, Institut Gustave Roussy, 94800 Villejuif, France, and Dr Saroj Gupta, Cancer Centre & Welfare Home, Thakurpukur, Calcutta-700 063, India.

MARGARET SNELLING

The 14th International Cancer Congress, Budapest, Hungary, August 21–27, 1986

There were over 7000 delegates from 79 countries attending the congress. On each of the five working days there were a multitude of scientific sessions to attend, but three one-hour long sessions (in the morning at 8.30 a.m., in the afternoon at 1.30 p.m. and in the evening at 6 p.m.) were simply devoted to plenary lectures when the whole conference was invited to listen to one single eminent specialist reviewing his area of interest. The titles of these lectures largely reflected current major interests and included "Advances in oncogene research", "The biochemical basis of cancer chemotherapy", "Monoclonal antibodies" and "The biology and epidemiology of retro viruses".

After the early plenary lecture there were between 12 and 19 simultaneous symposia every morning at each of which there were eight 20-minute presentations. In the afternoon there were 25 to 35 round-table or panel discussions which were really rather similar to the symposia, except that the presentations were limited to 15 minutes and 10 minutes, respectively. Finally, on each day there were some 40 poster sessions, with up to 20 posters in each which were discussed between 5 and 6 p.m. Each delegate was given a set of books weighing over 3 kg and containing over 5000 abstracts. With a programme of this size it was difficult for any one person to sample more than an insignificant proportion of the proceedings of the congress.

Subjects of special interest throughout the meeting must include: monoclonal antibodies, oncogenes, retro viruses, AIDS and interferon, with many sessions devoted to these subjects. There was a change in interest in cytotoxic chemotherapy from new drugs to new ways of using the old ones by modification of biological responses.

There were sessions on radiotherapy and radiobiology which reviewed broad areas of current interest such as: the causes of radioresistance, drug interaction, radiation damage and repair, radiation treatment planning and the use of neutrons, protons, pimesons and heavy particles. Some of these sessions went extremely well, bringing together experts in the field and generating some new information and useful discussion, while others were less satisfactory.

Of special interest was a lecture given by Dr Laszlo Lajtha on Hevesi's role in the development of nuclear medicine. It was fascinating to learn of this eminent Hungarian's international career and his many contributions to the science of nuclear medicine.

The arrangements for an enormous international meeting of this sort are, inescapably, complex and problems always arise. On the first day there were great difficulties because of the siting of 10 symposia under the same roof, with the sessions separated by thin, two-metre high partitions. A cacophony of sound led to an almost complete swamping of all communication and only with the greatest difficulty were these sessions completed. The organisers, however, quickly responded and with the use of an earphone system there was great improvement by the following day.

Social events were highlighted by an evening reception when the numbers were so great that those at the meeting had to be divided between the Houses of Parliament and the National Gallery. We all enjoyed the splendour of those buildings and the excellence of the wine and food. Most found Budapest to be a pleasant city, with good communications by the metro system and by the taxis which were, when the meters worked correctly, quite cheap. The congress was a good occasion to meet old friends and make new ones. Our Hungarian hosts went to great efforts to entertain us and we were all very grateful to them.

STANLEY DISCHE

Press releases

High sensitivity whole-body monitor for India

The Nuclear Enterprises whole-body monitor NE8114 uses blocks of NE110 plastic scintillator to achieve almost 3 π coverage of a human body, yielding a figure of merit of 44 cps per gram of potassium.

The system is to be supplied to the Institute of Nutrition, Hyderabad and was purchased by the UK Government's Overseas Development Agency to enable research to be carried out for the determination of the most efficient nutrition programmes for expectant and nursing mothers. By studying the incorporation of potassium and calcium, the ability of the mother to absorb proteins from the food she eats is determined. The system is so sensitive, it can rapidly measure the total potassium content of a baby—a measurement which is not readily achievable by any other system.

Philips Tomoscan on the move

As part of its on-going computed tomography (CT) programme, Philips Medical Systems has recently introduced the Philips mobile CT scanner, which comprises the Philips Tomoscan scanner installed in a purpose-built trailer. Supplied on a turn-key basis, the Philips Mobile Tomoscan scanner can be designed to users' specifications and is powered during operation by either direct link-up to the hospital's mains supply or by a separate diesel generator. The system is fully operational within 30 minutes of arrival on-site.

The first Philips mobile Tomoscan scanner in Europe was built to special order for the Clinica San Pio X of Milan, Italy. It uses a standard Philips Tomoscan scanner installed in a special vehicle, purpose-built by Smit Mobile Equipment B.V. in The Netherlands, under the supervision of Philips Medical Systems. The mobile scanner will be used by several hospitals within a 500 km radius of Milan and will be operated by a team of CT specialists from the Clinica San Pio X.

Further information is available from Philips, Postbus 523, 5600 AM Eindhoven, The Netherlands.

The Leukaemia Research Fund

The Fund has celebrated its Silver Jubilee—25 years in which great advances have been made in the successful treatment of leukaemia. A jubilee appeal target of £5 million has now been set to finance an intensive new programme of research, which it is hoped will make leukaemia the first cancer to be defeated.

This year has already seen the opening of two unique research centres at the Universities of Leeds and Glasgow to study the incidence and distribution of leukaemia and the role of viruses in human leukaemia. Further major research programmes are planned to look at genetic disposition to the disease and to improve treatments for both children and adults.

Library news

The BIR Library is open weekdays 9 a.m.–5 p.m. (7 p.m. on Thursdays)

The Librarian, Mrs Gunnel Ingham, is in attendance Tuesdays 11 a.m.–5 p.m., and Thursdays 11 a.m.–7 p.m., and Mrs Angela Lansdown, daily 9 a.m.–5 p.m. (Tel. 01-580 4085).

The journal stock includes more than 100 titles. Though journals may not be taken out of the library, there is a photocopy service, also available by post. A list of current journals is available on request and is also published in the March and September issues of the Bulletin.

Most books (excepting the historical collection) are available on loan.

Recent additions to the Library

BSI: Annual report 1985/86

Bolla, M., Racinet, C. & Vrousos, C. (Eds): Endometrial cancers. 1985

HPA: Measurement of the performance characteristics of diagnostic X-ray systems used in medicine. Part 5: Conventional tomographic equipment. 1985

Swallow, R. A. & Naylor, E. (Eds): Clark's positioning in radiography. 11th edit. 1986

Williams, C. J. & Whitehouse, J. M. A. (Eds): Cancer of the female reproductive system. 1985

Williams, E. D. (Ed.): An introduction to emission computed tomography. (IPSM report No. 44). 1985

Scientific document

EC Directive 84/466/Euratom: Draft regulation protection of persons undergoing medical examination or treatment regulations 1986. A copy of draft regulations and BIR comments are now filed in the Library.

ICR volumes wanted

The BIR Library possesses material from most (but not all) International Congresses of Radiology, but the Institute should have *all* these books and pamphlets. The librarian would be very grateful for help to fill the gaps.

BIR calendar events

Unless otherwise indicated, enquiries about the following events should be addressed to the Assistant Secretary: Programme, British Institute of Radiology, 36 Portland Place, London W1N 4AT (Tel. 01-580 4085).

The meetings are at 36 Portland Place unless otherwise stated. Attendance is open to non-members.

Practical Aspects of Magnetic Resonance Imaging

January 14, 1987 at 9.30 a.m.
Middlesex Hospital Medical School, London
Chairman: Professor I. Isherwood. Speakers: Dr M. Smith, Dr G. Bydder, Dr B. Kendall, Professor I. Isherwood, Dr J. P. R. Jenkins, Professor B. Worthington and Professor J. J. K. Best.
Joint BIR/RCR meeting.

Uroradiology Update

January 15, 1987 at 5.30 p.m.
Chairman: Dr D. Rickards. Speakers: Dr D. Rickards, Dr J. Pemberton, Dr C. E. L. Freer, Mr G. Watson, Dr R. Johnson, Dr W. Lees, Professor D. J. Allison.
Joint BIR/RCR/RSM meeting.

Radionuclide Investigations of the Lung

February 11, 1987
Joint IPSM/BIR (Nuclear Medicine Subcommittee) all day meeting organised by IPSM.

All day non-topic proffered papers meeting

February 13, 1987
Joint ARR/BIR (Radiobiology Subcommittee) meeting organised by the Association for Radiation Research.

Picture Archiving and Communications Systems

February 25, 1987 at 9.45 a.m.
Middlesex Hospital Medical School, London
Chairman: Professor I. Isherwood. Speakers: Mr D. Rothery, Mr C. Taylor, Dr W. Lees, Mr B. Bourne, Mr R. Vizy, Professor L. Gillanders, Mr H. Griffith, Mr P. Vernon, Mr C. Robertson, Mr Tiemann and Dr C. Greinacher.
Topics will include image display, image transmission and image storage.
All day meeting organised by Industry Committee.

Annual General Meeting

May 14, 1987 at 4.30 p.m.

Imaging in Radiotherapy

May 15, 1987
Chairmen: Dr D. Thwaites and another to be announced.
Joint IPSM/BIR all day meeting organised by IPSM.

Dysphagia and Disorders of Swallowing

May 20, 1987
Royal Society of Medicine, London
Joint RSM/RCR/BIR all day meeting to be organised by the RSM.

Conversazione

May 20, 1987
Royal Naval College, Greenwich

Advance Notice

British Institute of Radiology 45th Annual Congress, incorporating the joint BIR/RCR/RSM (Section of Radiology) spring meeting

RADIOLOGY '87

University of Southampton
April 1–3, 1987

The Congress will cover all aspects of radiology—X-ray diagnosis, radiotherapy, radiation oncology, nuclear medicine, ultrasound, NMR, radiological physics, radiobiology, radiation protection and related disciplines and is expected to include: •

The BIR Mackenzie Davidson Memorial Lecture, by Professor M. J. Peckham, "The clinical biology of testicular germ cell tumours"

The BIR Mayneord Lecture (sponsored by 3M UK plc), by Dr Frances Fry, "Chernobyl reactor accident—the impact on the United Kingdom"

The RCR George Simon Lecture, by Dr J. C. Batten, "Radiology and cystic fibrosis"

The BIR Presidential Address, by Professor R. J. Berry, "The Institute at 90—a time for reappraisal?"

The BIR Annual Dinner will be held at the Polygon Hotel, Southampton, on April 2.

For further information and registration forms please apply to the Assistant Secretary: Programme, The British Institute of Radiology, 36 Portland Place, London W1N 4AT (Tel. 01-580 4085).

Meetings and courses

As a service to our readers, the title, date and place of meetings and contact address will be inserted free of charge: any additional information will be charged at £1.75 per printed line, per insertion. Please contact the Managing Editor.

The British Medical Ultrasound Society 18th Annual Scientific Meeting
December 16–18, 1986
University of Warwick, Coventry
Further details: Mrs L. Blench, General Secretary, BMUS, 36 Portland Place, London W1N 3DG (Tel. 01-636 3714).

6th Conjoint Winter Meeting and the Technologist Section 14th Annual Meeting
January 30–February 4, 1987
San Antonio, Texas, USA
Further details: Education & Meetings Dept, Society of Nuclear Medicine, 136 Madison Avenue, New York 10016, USA (Tel. 212-889 0717).

Advanced Course in Diagnostic Imaging
February 8–13, 1987
Singapore
Further details: Professor Lenny Tan, Academy of Medicine, PO Box 694, Tiong Bahru Post Office, Singapore 9116, Republic of Singapore.

Radiation Transport Calculations Using EGS4
February 16–19, 1987
Ottawa, Canada
Further details: D. W. O. Rogers, Physics Division, NRCC, Ottawa, Ontario K1A 0R6, Canada (Tel. 613-993 2715).

The Bart's MCQ Course
February 21, 1987
St Bartholomew's Hospital, London
Further details: Miss V. Francis, MCQ Course Secretary, St Bartholomew's Hospital, X-ray Department, 4th Floor OPD, West Smithfield, London EC1A 7BE (Tel. 01-601 8303).

Positron Emission Tomography and the Chemistry of Mental Illness
March 12–13, 1987
Baltimore, Maryland
Further details: Pamela E. Macedonia, Program Coordinator, Turner 22, 720 Rutland Avenue, Baltimore, Maryland 21205, USA (Tel. 301-955 6085).

1987 European Workshop on Magnetic Resonance in Medicine
March 25–27, 1987
University College, London
Further details: Conference Secretariat, Magnetic Resonance in Medicine 1987, c/o Institute of Physical Sciences in Medicine, 47 Belgrave Square, London SW1X 8QX.

British Nuclear Medicine Society Annual Congress
April 12–15, 1987
Imperial College, London
Further details: Mrs A. Taylor, BNMS Conference Secretary, 22 Leinster Avenue, East Sheen, London SW14 7JP.

The Finzi Lecture
April 15, 1987
Royal Society of Medicine, London
"The solitary pulmonary nodule" by Dr S. Segalmann.
Further details: Royal Society of Medicine, 1 Wimpole Street, London W1M 8AE.

3rd European Symposium on Radiopharmacy and Radiopharmaceuticals
May 1–4, 1987
Elsinore, Denmark
Further details: Elisabeth Nørbygaard, The Isotope Pharmacy, 378 Frederikssundsvej, DK-2700 Brønshøj, Denmark.

Conference on Health Effects of Low Dose Ionising Radiation—Recent Advances and Their Implications
May 11–14, 1987
Royal Institute of British Architects, London
Further details: The Secretariat, British Nuclear Energy Society at the Institution of Civil Engineers, 1–7 Great George Street, London SW1P 3AA (Tel. 01-630 0726).

17th Annual Fleischner Society Symposium on Chest Disease
May 21–23, 1987
San Francisco, USA
Further details: Nomi Feldman, 3770 Tansy, San Diego, CA 92121, USA (Tel. 619-453 6222).

VI Congress of the European Association of Radiology (ECR '87)
May 31–June 6, 1987
Lisbon, Portugal
Further details: Secretariat ECR '87, SPRMN, Av. Elias Garcia, 123-7° DTo, 1000 Lisboa, Portugal, (Tel: 77-05 30, Telex 62074 SPRMN P).

Radiology of the Small Intestine
June 12, 1987
John Radcliffe Hospital, Oxford
Further details: Dr D. J. Nolan, Dept of Radiology, John Radcliffe Hospital, Oxford OX3 9DU (Tel. 0865-817 238).

College of Radiographers' Annual Conference
July 1–3, 1987
Scarborough
Further details: Miss C. Aldridge, College of Radiographers, 14 Upper Wimpole Street, London W1M 8BN (Tel. 01-935 5726, ext. 206).

XIVth Congress of the European Society of Neuroradiology
September 8–12, 1987
Udine, Italy
Further details: M. Leonardi, Servizio di Neuroradiologia, Ospedale Civile, 33100 Udine, Italy.

HPA Annual General Meeting and IPSM Scientific Meeting
September 15–19, 1987
Liverpool
Further details: IPSM, 47 Belgrave Square, London SW1X 8QX (Tel. 01-235 6111).

International School on Monte Carlo Transport of Electrons and Photons Below 50 MeV
September 24–October 3, 1987
Erice, Sicily
Further details: D. W. O. Rogers, Physics Division, NRCC, Ottawa, Ontario K1A 0R6, Canada (Tel. 613-993 2715) or A. E. Nahum, Physics Department, Royal Marsden Hospital, Sutton, Surrey SM2 5PT (Tel. 01-642 6011).

5th International Congress on the Ultrasonic Examination of the Breast
October 3–5, 1987
New Orleans, Louisiana
Further details: Department of Radiological Sciences, University of California Medical Center, Irvine, University Hospital, 101 City Drive South, Orange, California 92668, USA.

4th European Conference on Clinical Oncology and Cancer Nursing
November 1–4, 1987
Madrid, Spain
Further details: Siasa Congresos, Paseo de la Habana, 134, Madrid 28036, Spain (Tel. 457-4495).

RADIOLOGY '87

THE BRITISH INSTITUTE OF RADIOLOGY

RADIOLOGY '87
SOUTHAMPTON

45th Annual Congress and Exhibition, 1–3 April 1987

Incorporating the joint spring meeting of the Institute with the Royal College of Radiologists and the Section of Radiology of the Royal Society of Medicine.

The meeting will cover all aspects of the radiological sciences and a wide-ranging programme which will be of interest not only to radiologists, radiotherapists, radiographers and physicists but also to many others who are involved in or connected with radiology. Highlights include:

- BIR Presidential Address: Professor R J Berry
  The Institute at 90—A Time for Reappraisal?
- BIR Mackenzie Davidson Memorial Lecture: Professor M J Peckham
  The Clinical Biology of Testicular Germ Cell Tumours
- BIR Mayneord Lecture sponsored by 3M UK Plc: Dr F Fry
  Chernobyl Reactor Accident—The Impact on the United Kingdom
- RCR George Simon Lecture: Dr J C Batten
  Radiology and Cystic Fibrosis
- Poster and technical exhibition
- All day seminar
  Nuclear Reactor Accidents—Preparedness and Medical Consequences

For further information and registration details please apply to:

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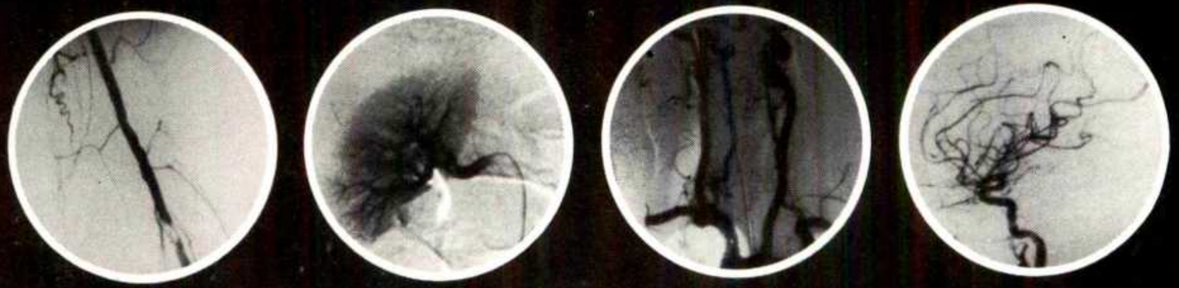

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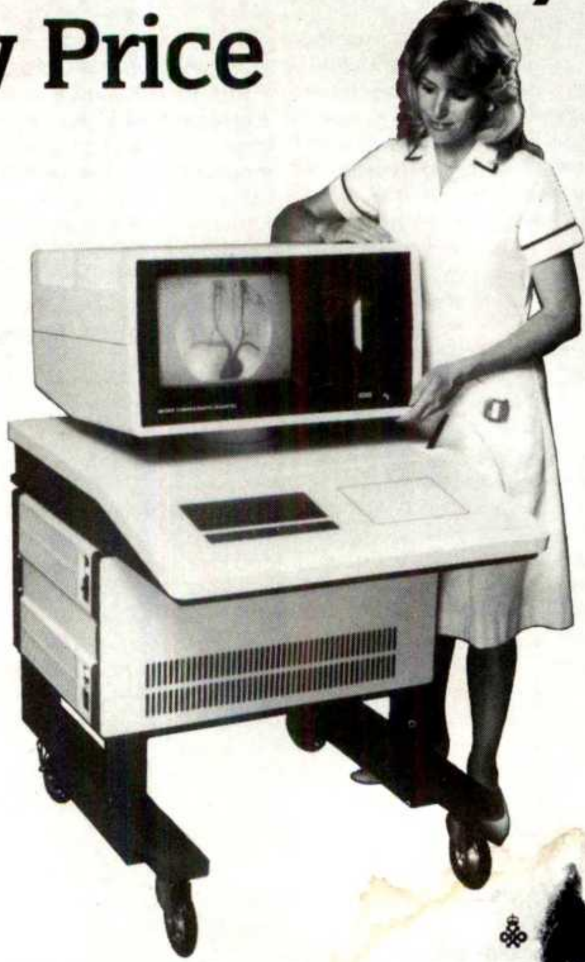

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Radiation Damage to Skin

Fundamentals and Practical Aspects

Proceedings of a Workshop held at Saclay, France, on October 9–11, 1985, organised by the Commission of the European Communities and the Commissariat à l'Energie Atomique de Protection et de Sûreté Nucléaire, Fontenay-aux-Roses, France.

Skin and underlying tissues are frequently critical structures in radiological protection. Over exposure to ionising radiation can cause serious long-term suffering and disability.

Despite their practical importance, the dose-effect relationships, the pathophysiological mechanisms and the influence of the degree to which different tissues are involved are still poorly understood.

This Workshop and Proceedings bring together those at the forefront of research in these areas from all over the world. They review the present state of knowledge and attempt to identify specific problem areas which may lead to recommendations for the improvement of radiological protection and for the better management of radiation accidents.

Radiation Damage to Skin is, therefore, a vital reference work for everyone working in radiation protection and dosimetry.

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About 200 pp.; illustrated

Orders to: The Publications Department, The British Institute of Radiology, 36 Portland Place, London W1N 3DG. Tel: 01-580 4085.

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